

The Medical Perspective on Environmental Sensitivities

Annotated Bibliography

- (1) Amdur MO, Doull J, Klaassen CD. *Casarett and Doull's toxicology: the basic science of poisons*. 4th ed. 1991.
Abstract: Textbook of toxicology
- (2) Lacour M, Zunder T, Schmidtke K, Vaith P, Scheidt C. Multiple chemical sensitivity syndrome (MCS)--suggestions for an extension of the U.S. MCS-case definition. *Int J Hyg Environ Health*. 2005;208:141-151.
Abstract: PURPOSE: To validate and extend the US case definition for the Multiple Chemical Sensitivity Syndrome (MCS) from 1999 by a systematic literature-review. DATA SOURCE: MEDLINE-research from 1997 to August 2003, research in the Cochrane-Library in August 2003, earlier reviews since 1997. STUDY SELECTION: Headings and abstracts were screened by one reviewer. All references dealing with multiple chemical sensitivities (MCS) which covered topics of interest such as symptom-profiles, differential diagnostic procedures, etc. were included in the analysis. DATA EXTRACTION AND SYNTHESIS: Topic-specific data extraction and synthesis was done by one reviewer. Data interpretation was discussed by all other authors. RESULTS: Out of 1429 references 36 publications proved to be suitable for the review. The results can be summarized as follows: exposure-related symptoms associated with self-reported multiple chemical sensitivities can be divided into non-specific complaints of the central nervous system--CNS (main characteristics) and functional disturbances in other organ systems (optional complaints). There is a significant overlap of MCS, CFS and fibromyalgia. At present no standards for a diagnostic procedure based on the criteria outlined above are existing CONCLUSIONS: MCS should only be diagnosed in patients who are mainly suffering from exposure-related non-specific complaints of the Central nervous system. The suggested diagnostic procedure follows the guidelines for CFS which are extended by diagnostic clarification of functional disturbances in other organ systems
- (3) Miller CS. The Compelling Anomaly of Chemical Intolerance. *Annals of the New York Academy of Sciences*. 2001;933:1-23.
- (4) Multiple chemical sensitivity: a 1999 consensus. *Arch Environ Health*. 1999;54:147-149.
Abstract: Consensus criteria for the definition of multiple chemical sensitivity (MCS) were first identified in a 1989 multidisciplinary survey of 89 clinicians and researchers with extensive experience in, but widely differing views of, MCS. A decade later, their top 5 consensus criteria (i.e., defining MCS as [1] a chronic condition [2] with symptoms that recur reproducibly [3] in response to low levels of exposure [4] to multiple unrelated chemicals and [5] improve or resolve when incitants are removed) are still unrefuted in published literature. Along with a 6th criterion that we now propose adding (i.e., requiring that symptoms occur in multiple organ systems), these criteria are all commonly encompassed by research definitions of MCS. Nonetheless, their standardized use in clinical settings is still lacking, long overdue, and greatly needed--especially in light of government studies in the United States, United Kingdom, and Canada that revealed 2-4 times as many cases of chemical sensitivity among Gulf War veterans than undeployed controls. In addition, state health department surveys of civilians in New Mexico and California showed that 2-6%, respectively, already had been diagnosed with MCS and that 16% of the civilians reported an "unusual sensitivity" to common everyday chemicals. Given this high prevalence, as well as the 1994 consensus of the American Lung Association,

American Medical Association, U.S. Environmental Protection Agency, and the U.S. Consumer Product Safety Commission that "complaints [of MCS] should not be dismissed as psychogenic, and a thorough workup is essential," we recommend that MCS be formally diagnosed--in addition to any other disorders that may be present--in all cases in which the 6 aforementioned consensus criteria are met and no single other organic disorder (e.g., mastocytosis) can account for all the signs and symptoms associated with chemical exposure. The millions of civilians and tens of thousands of Gulf War veterans who suffer from chemical sensitivity should not be kept waiting any longer for a standardized diagnosis while medical research continues to investigate the etiology of their signs and symptoms

- (5) McKeown-Eyssen GE, Baines CJ, Marshall LM, Jazmaji V, Sokoloff ER. Multiple chemical sensitivity: discriminant validity of case definitions. *Arch Environ Health*. 2001;56:406-412. Abstract: In this study, the authors used the University of Toronto's Health Survey self-administered questionnaire to determine discriminant validity of multiple chemical sensitivity definitions. The authors distributed a total of 4,126 questionnaires to adults who attended general, allergy, occupational, and environmental health practices. The authors then matched responses to features selected from existing case definitions posited by Thomson et al.; the National Research Council; Cullen; Ashford and Miller; Randolph; Nethercott et al.; and the 1999 Consensus (references 4-7, 2, 9, and 10, respectively, herein). The overall response rate was 61.7%. The prevalence of reported symptoms was lowest in general practices, was intermediate in occupational health and allergy practices, and was highest in environmental health practices. Features from the definitions presented by Nethercott et al. and the 1999 Consensus (references 9 and 10, respectively, herein) correctly identified more than 80% of environmental health practice patients and more than 70% of general practice patients. Combinations of 4 symptoms (i.e., having a stronger sense of smell than others, feeling dull/groggy, feeling "spacey," and having difficulty concentrating) also discriminated successfully. In summary, features from 2 of 7 case definitions assessed by the University of Toronto Health Survey achieved good discrimination and identified patients with an increased likelihood of multiple chemical sensitivity
- (6) Johansson O. Electrohypersensitivity: State-of-the-Art of a Functional Impairment. *Electromagn Biol Med*. 2006;25:245-258. Abstract: Recently, a new category of persons, claiming to suffer from exposure to electromagnetic fields, has been described in the literature. In Sweden, electrohypersensitivity (EHS) is an officially fully recognized functional impairment (i.e., it is not regarded as a disease). Survey studies show that somewhere between 230,000-290,000 Swedish men and women report a variety of symptoms when being in contact with electromagnetic field (EMF) sources. The aim of our studies has been to investigate possible alterations, in the cellular and neuronal systems of these person' skin. As controls, age- and sex-matched persons, without any subjective or clinical symptoms or dermatological history, served. Immunohistochemistry using antisera to the previously characterized marker substances of interest has been utilized. In summary, it is evident from our preliminary data that various alterations are present in the electrohypersensitive person' skin. In view of recent epidemiological studies, pointing to a correlation between long-term exposure from power-frequent magnetic fields or microwaves and cancer, our data ought to be taken seriously and further analyzed
- (7) Bailey WH. Health effects relevant to the setting of EMF exposure limits. *Health Phys*. 2002;83:376-386. Abstract: To date, electric and magnetic exposure limits for frequencies below 100 kHz have

been based on vaguely defined neurobiological responses to electric fields induced in tissues in vivo by magnetic fields and on perceptual responses to external electric fields. Advances in tissue dosimetry, risk assessment methods, and biological research on stimulation thresholds and mechanisms are providing new bases for exposure limits. This paper reviews the historical basis for current electric and magnetic exposure limits in preparation for the development of the "next generation" of electric and magnetic occupational and public exposure guidelines. This is followed by an overview of reported neurobiological effects of electric and magnetic stimulation that should be considered in new exposure guidelines. For magnetic fields, there is stronger evidence for setting exposure limits to protect against adverse effects of nerve stimulation than for protecting against visual magnetophosphenes. Magnetophosphenes are not adverse, and the evidence that these perceptual responses of the eye are a precursor or surrogate for other adverse neurologic responses is weak. Rather than relying just on theoretical models to set exposure limits, data from human subjects exposed to pulsed magnetic fields should be used to estimate nerve stimulation thresholds. Such data can provide a solid basis for setting magnetic field exposure limits if uncertainties in the data and inter-individual variability are addressed. Research on sensory perception, spontaneous and evoked potentials, and epidemiologic studies of neuropsychiatric conditions in electric and magnetic exposed populations does not suggest a need for lower exposure limits. However, a report that a 60-mT magnetic field (below the threshold for peripheral nerve stimulation) produces prolonged alterations of brain excitability and "indisposure" of subjects should be investigated in future research

- (8) Havas M. Electromagnetic hypersensitivity: biological effects of dirty electricity with emphasis on diabetes and multiple sclerosis. *Electromagn Biol Med.* 2006;25:259-268.
Abstract: Dirty electricity is a ubiquitous pollutant. It flows along wires and radiates from them and involves both extremely low frequency electromagnetic fields and radio frequency radiation. Until recently, dirty electricity has been largely ignored by the scientific community. Recent inventions of metering and filter equipment provide scientists with the tools to measure and reduce dirty electricity on electrical wires. Several case studies and anecdotal reports are presented. Graham/Stetzer (GS) filters have been installed in schools with sick building syndrome and both staff and students reported improved health and more energy. The number of students needing inhalers for asthma was reduced in one school and student behavior associated with ADD/ADHD improved in another school. Blood sugar levels for some diabetics respond to the amount of dirty electricity in their environment. Type 1 diabetics require less insulin and Type 2 diabetics have lower blood sugar levels in an electromagnetically clean environment. Individuals diagnosed with multiple sclerosis have better balance and fewer tremors. Those requiring a cane walked unassisted within a few days to weeks after GS filters were installed in their home. Several disorders, including asthma, ADD/ADHD, diabetes, multiple sclerosis, chronic fatigue, fibromyalgia, are increasing at an alarming rate, as is electromagnetic pollution in the form of dirty electricity, ground current, and radio frequency radiation from wireless devices. The connection between electromagnetic pollution and these disorders needs to be investigated and the percentage of people sensitive to this form of energy needs to be determined
- (9) Park J and Knudson S. Medically unexplained physical symptoms. Statistics Canada . 12-1-2007. <http://www.statcan.ca/english/freepub/82-003-XIE/2006001/articles/symptoms/82-003-XIE2006002.pdf> available from <http://www.statcan.ca/english/freepub/82-003-XIE/82-003-XIE2006001.htm>
Abstract: A substantial number of Canadians report symptoms of conditions that cannot be

definitively identified through physical examination or medical testing. Known as "medically unexplained physical symptoms," or "MUPS," they characterize conditions such as chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivity. The lack of consistent explanations from physical and laboratory assessments has caused confusion and controversy about these conditions. Many people, including some health care professionals, do not believe that these conditions exist, attributing the symptoms to a variety of other causes. However, for the people who are affected, the symptoms are real and frequently debilitating. Based on information from the 2002 and 2003 Canadian Community Health Survey (CCHS), this article describes the prevalence of MUPS and the characteristics of Canadians who report having these conditions. It also examines co-morbidity with psychiatric disorders, and associations with dependency, self-perceived mental health, and the use of health care services.

- (10) Statistics Canada, Health Statistics Division. How healthy are Canadians? Health Reports - Supplement to Volume 16 catalogue no. 820003-XPE. 2006. Canadian Institute for Health Information. Health Reports. <http://dsp-psd.pwgsc.gc.ca/Collection/Statcan/82-003-S/82-003-SIE2005000.pdf>
- (11) Statistics Canada. Findings from the 2005 National Survey of the Work and Health of Nurses. Statistics Canada . 11-12-2006. <http://www.statcan.ca/english/freepub/83-003-XIE/83-003-XIE2006001.pdf> available from <http://www.statcan.ca/cgi-bin/downpub/listpub.cgi?catno=83-003-XIE2006001>

Abstract: Prevalence of Multiple Chemical Sensitivities (%)

N.L. 5.9

P.E.I. 3.8

N.S. 5.4

N.B. 4.0

Que. 1.0

Ont. 3.7

Man. 5.3

Sask. 6.2

Alta. 4.5

B.C. 5.9

Y.T., N.W.T., Nvt. 3.7

- (12) Caress SM, Steinemann AC. A review of a two-phase population study of multiple chemical sensitivities. *Environ Health Perspect.* 2003;111:1490-1497.
 Abstract: In this review we summarize the findings of a two-phase study of the prevalence, symptomatology, and etiology of multiple chemical sensitivities (MCS). We also explore possible triggers, the potential linkage between MCS and other disorders, and the lifestyle alterations produced by MCS. The first phase of the study consisted of a random sampling of 1,582 individuals from the Atlanta, Georgia, metropolitan area to determine the reported prevalence of a hypersensitivity to common chemicals. In this phase, 12.6% of the sample reported a hypersensitivity. Further questioning of individuals with a hypersensitivity indicated that 13.5% (1.8% of the entire sample) reported losing their jobs because of their hypersensitivity. The second phase was a follow-up questioning of the respondents who initially reported hypersensitivity. In this phase, we found that individuals with hypersensitivity experience a variety of symptoms and triggers. A significant percentage (27.5%) reported that their hypersensitivity was initiated by an exposure to pesticides, whereas an equal percentage (27.5%) attributed it to solvents. Only 1.4% had a history of prior emotional problems, but

37.7% developed these problems after the physical symptoms emerged. This suggests that MCS has a physiologic and not a psychologic etiology

- (13) Kreutzer R, Neutra RR, Lashuay N. Prevalence of people reporting sensitivities to chemicals in a population-based survey. *Am J Epidemiol.* 1999;150:1-12.
Abstract: To describe the prevalence and correlates of reports about sensitivities to chemicals, questions about chemical sensitivities were added to the 1995 California Behavior Risk Factor Survey (BRFS). The survey was administered by telephone to 4,046 subjects. Of all respondents, 253 (6.3%) reported doctor-diagnosed "environmental illness" or "multiple chemical sensitivity" (MCS) and 643 (15.9%) reported being "allergic or unusually sensitive to everyday chemicals." Sensitivity to more than one type of chemical was described by 11.9% of the total sample population. Logistic regression models were constructed. Hispanic ethnicity was associated with physician-diagnosed MCS (adjusted odds ratio (OR) = 1.82, 95% confidence interval (CI) 1.21-2.73). Female gender was associated with individual self-reports of sensitivity (adjusted OR = 1.63, 95% CI 1.23-2.17). Marital status, employment, education, geographic location, and income were not predictive of reported chemical sensitivities or reported doctor diagnosis. Surprising numbers of people believed they were sensitive to chemicals and made sick by common chemical exposures. The homogeneity of responses across race-ethnicity, geography, education, and marital status is compatible with a physiologic response or with widespread societal apprehensions in regard to chemical exposure
- (14) Caress SM, Steinemann AC. National prevalence of asthma and chemical hypersensitivity: an examination of potential overlap. *J Occup Environ Med.* 2005;47:518-522.
Abstract: OBJECTIVE: The objective of this study was to investigate the linkage between asthma and chemical hypersensitivity. METHODS: The authors conducted a population study with a random sample of 1057 geographically weighted cases to determine the prevalence of both asthma and chemical hypersensitivity in the American population and to explore their co-occurrence. RESULTS: A total of 14.1% of the respondents reported being diagnosed with asthma and 11.2% reported a hypersensitivity to chemicals. Of those with asthma, 27.2% also reported being hypersensitive to chemicals and 7.4% reported also being diagnosed with multiple chemical sensitivities (MCS). Of those diagnosed with MCS, 42% reported also being diagnosed with asthma. Additionally, 29.7% of those with asthma said air fresheners caused breathing difficulties, and 37.2% found scented products irritating. CONCLUSIONS: The results indicate that there is significant overlap between some forms of asthma and chemical hypersensitivity
- (15) Meggs WJ, Dunn KA, Bloch RM, Goodman PE, Davidoff AL. Prevalence and nature of allergy and chemical sensitivity in a general population. *Arch Environ Health.* 1996;51:275-282.
Abstract: The objectives of this study were (a) to determine the self-reported prevalence of allergy and chemical sensitivity in a rural population of eastern North Carolina, (b) to determine the type and frequency of symptoms for each condition, and (c) to determine the demographic groups affected. A random general telephone survey was conducted during the period May 14, 1993, to September 10, 1993, and questions about allergy and chemical sensitivity were asked. Of the 1 446 households contacted, 1 027 (71%) individuals agreed to participate. Allergies were reported by 365 (35%) individuals. Thirty percent of allergic individuals reported that symptoms occurred once or more each week, whereas 61% reported that symptoms occurred, at most, once each month. Allergic symptoms that occurred daily were reported by 5.3% of the total population. Chemical sensitivity was reported by 336 (33%) individuals. Thirty-five per cent of chemically sensitive individuals reported symptoms at least once each week, whereas

53% reported that symptoms occurred once (or less) each month. Symptoms of chemical sensitivity that occurred daily were reported by 3.9% of the total population. Both allergy and chemical sensitivity were distributed widely across age, income, race, and educational groups. Simultaneous allergy and chemical sensitivity were reported by 16.9% of the population, allergy without chemical sensitivity by 16.0%, chemical sensitivity without allergy by 18.2%, and neither condition by 48.9%. If the prevalence of sensitivity to chemical irritants is, in fact, equivalent to that of allergy, as was found in this study, then support for the scientific investigation of chemical sensitivity is justified

- (16) McKeown-Eyssen G, Baines C, Cole DE et al. Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR. *Int J Epidemiol.* 2004;33:971-978.

Abstract: BACKGROUND: Impaired metabolism of toxic chemicals is a postulated mechanism underlying multiple chemical sensitivity (MCS). Because genetic variation alters the rate of chemical metabolism, this study was designed to determine if MCS cases differed from controls for genetic polymorphisms in drug-metabolizing enzymes. METHODS: Female Caucasian participants (203 cases and 162 controls) were drawn from a larger case-control study based on a reproducible and validated case definition. Common polymorphisms for CYP2D6, NAT1, NAT2, PON1, and PON2 were genotyped. RESULTS: Comparing cases and controls, significant differences were found in genotype distributions for CYP2D6 ($P = 0.02$) and NAT2 ($P = 0.03$). Compared with the referent homozygous inactive (CYP2D6) or slow (NAT2) metabolizers, the odds for being CYP2D6 homozygous active ($OR = 3.36$, $P = 0.01$) and NAT2 rapid ($OR = 4.14$, $P = 0.01$) were significantly higher in cases than controls. The odds for being heterozygous for PON1-55 ($OR = 2.05$, $P = 0.04$) and PON1-192 ($OR = 1.57$, $P = 0.04$) were also significantly higher in cases. CONCLUSIONS: A genetic predisposition for MCS may involve altered biotransformation of environmental chemicals. The CYP2D6 enzyme activates and inactivates toxins; the NAT2 enzyme bioactivates arylamines to protein-binding metabolites. A gene-gene interaction between CYP2D6 and NAT2 suggested that rapid metabolism for both enzymes may confer substantially elevated risk ($OR = 18.7$, $P = 0.002$). Our finding parallels others' observation of a link between PON1 heterozygosity and neurological symptoms in Gulf War syndrome. This first demonstration of genetic variation in drug-metabolizing enzymes in association with MCS requires replication. However, it suggests new research directions on genetically variable toxin pathways that might be important in MCS

- (17) Costa LG, Richter RJ, Li WF, Cole T, Guizzetti M, Furlong CE. Paraoxonase (PON 1) as a biomarker of susceptibility for organophosphate toxicity. *Biomarkers.* 2003;8:1-12.

Abstract: Paraoxonase (PON1) is an A-esterase capable of hydrolysing the active metabolites (oxons) of a number of organophosphorus (OP) insecticides such as parathion, diazinon and chlorpyrifos. PON1 activity is highest in liver and plasma, and among animal species significant differences exist, with birds and rabbits displaying very low and high activity, respectively. Human PON1 has two polymorphisms in the coding region (Q192R and L55M) and five polymorphisms in the promoter region. The Q192R polymorphism imparts different catalytic activity toward some OP substrates, while the polymorphism at position -108 (C/T) is the major contributor to differences in the level of PON1 expression. Animal studies have shown that PON1 is an important determinant of OP toxicity, with animal species with a low PON1 activity having an increased sensitivity to OPs. Administration of exogenous PON1 to rats or mice protects them from the toxicity of OPs. PON1 knockout mice display a high sensitivity to the toxicity of diazoxon and chlorpyrifos oxon, but not paraoxon. In vitro assayed catalytic efficiencies of purified PON(192) isoforms for hydrolysis of specific oxon substrates

accurately predict the degree of in vivo protection afforded by each isoform. Low PON1 activity may also contribute to the higher sensitivity of newborns to OP toxicity

- (18) Furlong CE, Cole TB, Jarvik GP et al. Role of paraoxonase (PON1) status in pesticide sensitivity: genetic and temporal determinants. *Neurotoxicology*. 2005;26:651-659.
Abstract: Individual differences in detoxication capacities for specific organophosphorous (OP) compounds are due largely to differences in catalytic efficiency or abundance of the HDL-associated enzyme, paraoxonase (PON1). First, we provide evidence that children less than 2 years of age represent a particularly susceptible population for OP exposure due to low abundance of PON1 and variable onset of plasma PON1 activity. Second, we describe studies examining the neurotoxic effects of chronic, low-level OP pesticide exposure in mice. PON1 knockout (PON1(-/-)) and wild-type mice were exposed chronically (PN4 to PN21) to low levels of chlorpyrifos oxon (CPO). Endpoints included cholinesterase activity, histopathology, gene expression, and behavior. Even at PN4, when PON1 levels were low in wild-type mice, PON1(-/-) mice were more sensitive to inhibition of brain cholinesterase by CPO. At PN22, and persisting as long as 4 months, chronic developmental exposure to 0.18 mg/kg/d or 0.25 mg/kg/d CPO resulted in perinuclear vacuolization of cells in a discrete area of the neocortex and irregular distribution of neurons in the cortical plate, with an increase in the number of affected cells at 0.25mg/kg/d. Third, we describe a transgenic mouse model in which human transgenes encoding either hPON1Q192 or hPON1R192 were expressed at equal levels in place of mouse PON1. The developmental onset of expression followed the mouse time course and was identical for the two transgenes, allowing these mice to be used to assess the importance of the Q192R polymorphism during development. Adult mice expressing hPON1R192 were significantly more resistant than hPON1Q192 mice to CPO toxicity. Our studies indicate that children less than 2 years old, especially those homozygous for PON1Q192, would be predicted to be particularly susceptible to CPO toxicity
- (19) Cole TB, Jampsa RL, Walter BJ et al. Expression of human paraoxonase (PON1) during development. *Pharmacogenetics*. 2003;13:357-364.
Abstract: BACKGROUND: Paraoxonase (PON1), a HDL-associated enzyme, protects against toxicity from specific organophosphorus compounds and oxidized lipids. Common polymorphisms in the PON1 gene have been identified and characterized in the coding region, 5' regulatory region and 3' UTR. The Q192R coding region polymorphism determines substrate-dependent differences in catalytic efficiency of hydrolysis. The -108CT polymorphism in the 5' regulatory region has a significant effect on PON1 expression, with the -108C allele expressing on average twice the level of plasma PON1 as the -108T allele. In addition to the effects of regulatory and coding region polymorphisms on PON1 levels and activity, plasma PON1 levels are also developmentally regulated. Since PON1 levels are important in determining resistance to specific organophosphorus compounds, the time course of appearance of PON1 in newborns is of great interest. RESULTS: We report here that PON1 levels plateau between 6 to 15 months of age, and that variability in the age at which PON1 levels plateau is quite variable among individuals. In mice and rats, plasma PON1 activity reaches a plateau at 3 weeks of age. In mice that lack endogenous PON1, human transgenes encoding either PON1(Q192) or PON1(R192) under the control of the human PON1 regulatory sequences exhibited a similar time course of expression as that seen in wild-type mice, indicating conservation of the developmental regulatory elements between mouse and human PON1
- (20) Haley RW, Billecke S, La Du BN. Association of low PON1 type Q (type A) arylesterase activity with neurologic symptom complexes in Gulf War veterans. *Toxicol Appl Pharmacol*.

1999;157:227-233.

Abstract: Previously Haley et al. described six possible syndromes identified by factor analysis of symptoms in Gulf War veterans and demonstrated that veterans with these symptom complexes were more neurologically impaired than age-sex-education-matched well controls. They also uncovered strong associations (relative risks 4-8) suggesting that these symptom complexes were related to wartime exposure to combinations of organophosphate pesticides, chemical nerve agents, high concentration DEET insect repellent, and symptoms of advanced acute toxicity after taking pyridostigmine. Here we have shown that compared to controls, ill veterans with the neurologic symptom complexes were more likely to have the R allele (heterozygous QR or homozygous R) than to be homozygous Q for the paraoxonase/arylesterase 1 (PON1) gene. Moreover, low activity of the PON1 type Q (Gln192, formerly designated type A) arylesterase allozyme distinguished ill veterans from controls better than just the PON1 genotype or the activity levels of the type R (Arg192, formerly designated type B) arylesterase allozyme, total arylesterase, total paraoxonase, or butyrylcholinesterase. A history of advanced acute toxicity after taking pyridostigmine was also correlated with low PON1 type Q arylesterase activity. Type Q is the allozyme of paraoxonase/arylesterase that most efficiently hydrolyzes several organophosphates including sarin, soman, and diazinon. These findings further support the proposal that neurologic symptoms in some Gulf War veterans were caused by environmental chemical exposures

- (21) La Du BN, Billecke S, Hsu C, Haley RW, Broomfield CA. Serum paraoxonase (PON1) isozymes: the quantitative analysis of isozymes affecting individual sensitivity to environmental chemicals. *Drug Metab Dispos.* 2001;29:566-569.

Abstract: In a recent study on Gulf War veterans who developed delayed neurotoxicity symptoms, we found their levels of serum paraoxonase (PON1) isozyme type Q to be significantly lower than in the control, unaffected veteran group. These results were obtained in 25 ill veterans and 20 well control subjects, of which 10 were deployed and 10 were nondeployed battalion members who remained in the United States during the Gulf War. The blood samples were also assayed for serum butyrylcholinesterase in our laboratory, and more recently in Dr. C. Broomfield's laboratory for somanase and sarinase activities. The cholinesterase activities showed no significant correlation with the PON1 isozyme levels or the severity of the clinical symptoms, but the somanase and sarinase levels ran parallel to the PON1 type Q isozyme concentrations. Although there is no direct evidence that these Gulf War veterans were directly exposed to or encountered either of these nerve gases, they may have been exposed to some environmental or chemical toxin with a similar preference for hydrolysis by the PON1 type Q isozyme. The number of subjects is relatively small, but the results should encourage other investigators to examine both the individual phenotypes and the levels of PON1 isozymes in other groups exhibiting neurological symptoms

- (22) Schnakenberg E, Fabig KR, Stanulla M et al. A cross-sectional study of self-reported chemical-related sensitivity is associated with gene variants of drug metabolizing enzymes. *Environ Health.* 2007;6:6.

Abstract: ABSTRACT: BACKGROUND: N-acetyltransferases (NAT) and glutathione S-transferases (GST) are involved in the metabolism of several ubiquitous chemical substances leading to the activation and detoxification of carcinogenic heterocyclic and aromatic amines. Since polymorphisms within these genes are described to influence the metabolism of ubiquitous chemicals, we conducted the present study to determine if individuals with self-reported chemical-related sensitivity differed from controls without self-reported chemical-related sensitivity with regard to the distribution of genotype frequencies of NAT2, GSTM1,

GSTT1, and GSTP1 polymorphisms. Methods: Out of 800 subjects who answered a questionnaire of ten items with regard to their severity of chemical sensitivity 521 unrelated individuals agreed to participate in the study. Subsequently, genetic variants of the NAT2, GSTM1, GSTT1, and GSTP1 genes were analyzed. Results: The results show significant differences between individuals with and without self-reported chemical-related sensitivity with regard to the distribution of NAT2, GSTM1, and GSTT1 gene variants. Cases with self-reported chemical-related sensitivity were significantly more frequently NAT2 slow acetylators (controlled OR = 1.81, 95% CI = 1.27-2.59, P = 0.001). GSTM1 and GSTT1 genes were significantly more often homozygously deleted in those individuals reporting sensitivity to chemicals compared to controls (GSTM1: controlled OR 2.08, 95% CI= 1.46-2.96, P = 0.0001; GSTT1: controlled OR = 2.80, 95% CI= 1.65-4.75, P = 0.0001). Effects for GSTP1 gene variants were observed in conjunction with GSTM1, GSTT1 and NAT2 gene. Conclusions: The results from our study population show that individuals being slow acetylators and/or harbouring a homozygous GSTM1 and/or GSTT1 deletion reported chemical-related hypersensitivity more frequently

- (23) Baines CJ, McKeown-Eyssen GE, Riley N et al. Case-control study of multiple chemical sensitivity, comparing haematology, biochemistry, vitamins and serum volatile organic compound measures. *Occup Med (Lond)*. 2004;54:408-418.
Abstract: BACKGROUND: Multiple chemical sensitivity (MCS), although poorly understood, is associated with considerable morbidity. AIM: To investigate potential biological mechanisms underlying MCS in a case-control study. METHODS: Two hundred and twenty-three MCS cases and 194 controls (urban females, aged 30-64 years) fulfilled reproducible eligibility criteria with discriminant validity. Routine laboratory results and serum levels of volatile organic compounds (VOCs) were compared. Dose-response relationships, a criterion for causality, were examined linking exposures to likelihood of case status. RESULTS: Routine laboratory investigations revealed clinically unimportant case-control differences in means. Confounder-adjusted odds ratios (OR) showed MCS was negatively associated with lymphocyte count and total plasma homocysteine, positively associated with mean cell haemoglobin concentration, alanine aminotransferase and serum vitamin B6, and not associated with thyroid stimulating hormone, folate or serum vitamin B12. More cases than controls had detectable serum chloroform (P = 0.001) with the OR for detectability 2.78 (95% confidence interval = 1.73-4.48, P < 0.001). Chloroform levels were higher in cases. However, cases had significantly lower means of detectable serum levels of ethylbenzene, m&p-xylene, 3-methylpentane and hexane, and means of all serum levels of 1,3,5- and 1,2,3-trimethylbenzene, 2- and 3-methylpentane, and m&p-xylene. CONCLUSIONS: Our findings are inconsistent with proposals that MCS is associated with vitamin deficiency or thyroid dysfunction, but the association of lower lymphocyte counts with an increased likelihood of MCS is consistent with theories of immune dysfunction in MCS. Whether avoidance of exposures or different metabolic pathways in cases explain the observed lower VOC levels or the higher chloroform levels should be investigated
- (24) Miller CS, Gammage RB, Jankovic JT. Exacerbation of chemical sensitivity: a case study. *Toxicol Ind Health*. 1999;15:398-402.
Abstract: We report exacerbation of symptoms and chemical intolerances in three of four self-described chemically sensitive women following relocation to a newly constructed office building. Levels of total volatile organic compounds (TVOCs) in this building prior to occupancy were approximately 200 micrograms/m³ (toluene equivalent units) with a myriad of individual components present. By day 50 after occupancy, the concentration of TVOCs in the

building dropped to approximately 50 micrograms/m³. Nevertheless, three women reported significant worsening of their symptoms with spreading of their sensitivities to previously tolerated chemical exposures. One woman relocated to another building, while the other two managed their symptoms by reducing time spent in the building or by using a room air cleaner. By day 600 following occupancy, although TVOCs had increased significantly (perhaps due to cleaning agents), there were fewer individual VOCs present in the air, and some of the women were able to tolerate the air in the building. We conclude that complex mixtures of VOCs at very low levels tolerated by the majority of building occupants may pose problems for persons who report pre-existing chemical sensitivities. TVOC measurements may not correlate with symptoms in these individuals. Reasonable accommodations by an employer can reduce problem exposures, making it possible for some affected individuals to continue productive employment

- (25) Brasche S, Bullinger M, Morfeld M, Gebhardt HJ, Bischof W. Why do women suffer from sick building syndrome more often than men?--subjective higher sensitivity versus objective causes. *Indoor Air*. 2001;11:217-222.

Abstract: Office workers often report so-called sick building syndrome (SBS) symptoms affecting the skin, mucous membranes and nervous system. The recurring higher prevalence of SBS in women was investigated using questionnaire and ergonomic data from the German ProKlimA-Project. The hypothesis that working conditions and job characteristics for women are inferior to those of men was tested for groups of risk factors. Finally, gender-specific multiple logistic regression models were compared. It was found that 44.3% of women (n = 888) and 26.2% of men (n = 576) suffer SBS with significant differences between men and women for many variables. Considering sub-groups--supposing the same circumstances in psycho-social and work-related conditions--gender-specific SBS prevalence rates differ as for the whole sample, e.g. 35.9% of women with the most favourable job characteristic suffer SBS (men: 19.4%), 53.0% of women with the most unfavourable job characteristic suffer SBS (men: 33.3%). These results show that women suffer more SBS than men independent of personal, most work-related and building factors. Multiple logistic models define self-reported acute illness, job satisfaction, software quality and job characteristics as significant gender-independent risk factors. Number of persons/room, self-reported allergy and smoking are characteristic female risk factors. Age is a significant risk factor only in men

- (26) McKeown-Eyssen GE, Sokoloff ER, Jazmaji V, Marshall LM, Baines CJ. Reproducibility of the University of Toronto self-administered questionnaire used to assess environmental sensitivity. *Am J Epidemiol*. 2000;151:1216-1222.

Abstract: Environmental sensitivity patients report symptoms provoked by low-level exposure to a wide range of substances. Features of published case definitions include nature of onset, chronicity, symptom provocation by multiple substances, symptom provocation by an escalating number of exposures, involvement of multiple body systems including the nervous system, provocation by unrelated substances, and addictive behaviors. This study assessed the reproducibility of a Canadian self-administered questionnaire, the University of Toronto Health Survey, designed to determine the prevalence of the features described in these case definitions. A total of 191 eligible respondents aged 16-70 years who attended several types of medical practices in 1994 were invited to complete a second questionnaire 5-7 months after the first; 134 (70.2%) complied. Total agreement on whether patients satisfied each of seven case definitions ranged from 80% to 90%. After adjustment for chance, major agreement was observed for three of the seven case definitions ($\kappa = 0.69, 0.68, \text{ and } 0.78$). The survey

achieved good reproducibility regarding self-report of symptoms described in published case definitions of environmental sensitivity

- (27) Joffres MR, Williams T, Sabo B, Fox RA. Environmental sensitivities: prevalence of major symptoms in a referral center: the Nova Scotia Environmental Sensitivities Research Center Study. *Environ Health Perspect.* 2001;109:161-165.
Abstract: Although the phenomenon of environmental sensitivities (ES) has no clear etiology nor well-accepted pathophysiology, affected individuals experience symptoms that cause varying levels of dysfunction. Through a dedicated, government-funded research and treatment center, a detailed questionnaire covering 217 symptoms in 13 systems was mailed in 1997-1998 to 812 individuals referred to the center by physicians. A total of 385 (47%) questionnaires were returned, and data were analyzed on 351 individuals. Participants tended to be women (80%), middle-aged individuals (37% age 40-49 years), and those in higher educational groups (28% completed university), but there was wide variation in demographic variables. General symptoms such as difficulty concentrating, fatigue, forgetfulness, and irritability dominated the overall prevalence of symptoms since the start of their illness. Those related to irritation such as sneezing, itchy or burning eyes, and hoarseness or loss of voice were more common after exposure to environmental irritants. Ranking of symptoms using severity scores was consistent between men and women. Overall scores were higher in women, in participants who were separated or divorced, and in low-income groups. The type and consistency of symptoms experienced after exposure to triggering substances may not fit a purely psychogenic theory
- (28) Gibson PR, Elms AN, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity. *Environ Health Perspect.* 2003;111:1498-1504.
Abstract: Multiple chemical sensitivity (MCS) is a condition in which persons experience negative health effects in multiple organ systems from exposure to low levels of common chemicals. Although symptoms experienced from particular chemicals vary across persons, they are generally stable within persons. The sensitivities often spread over time, first to related chemicals and then to other classes of chemicals. This study examined self-reported perceived treatment efficacy of 101 treatments used by 917 persons with self-reported MCS. Treatments examined included environmental medicine techniques, holistic therapies, individual nutritional supplements, detoxification techniques, body therapies, Eastern-origin techniques, newer therapies, prescription items, and others. The three most highly rated treatments were creating a chemical-free living space, chemical avoidance, and prayer. Both creating a chemical-free living space and chemical avoidance were rated by 95% of respondents as helpful. Results for most therapies were mixed. Participants had consulted a mean of 12 health care providers and spent over one-third of their annual income on health care costs. We discuss this drain on personal resources and describe respondents' attitudes toward the possibility of healing from MCS
- (29) Caress SM, Steinemann AC, Waddick C. Symptomatology and etiology of multiple chemical sensitivities in the southeastern United States. *Arch Environ Health.* 2002;57:429-436.
Abstract: A questionnaire was administered to individuals who had reported a hypersensitivity to common chemical products in an earlier epidemiological study in the Atlanta, Georgia, metropolitan area. The questionnaire investigated the nature of the symptoms and factors that potentially initiated hypersensitivity and subsequently triggered reactions. Also examined were associated lifestyle modifications and the relationships of hypersensitivity with other illnesses. The authors found that a majority of hypersensitive individuals (52.2%) experienced either

"severe" or "somewhat severe" symptoms. The most common triggers of symptoms were cleaning products (88.4%), tobacco smoke (82.6%), perfume (81.2%), pesticides (81.2%), and car exhaust (72.5%). Only 1.4% of the subjects had a prior history of emotional problems, whereas 37.7% developed such problems after the emergence of their hypersensitivity. Lifestyle modifications varied; 76.8% changed their household cleaning/personal hygiene products, 47.8% began using water and/or air filtration systems, and 13% found it necessary to change residence. Although hypersensitivity was more common in females than males, the condition affects individuals in all categories of race/ethnicity, age, household income, and educational level

- (30) Caress SM, Steinemann AC. Prevalence of multiple chemical sensitivities: a population-based study in the southeastern United States. *Am J Public Health*. 2004;94:746-747.
Abstract: We examined the prevalence of multiple chemical sensitivities (MCS), a hypersensitivity to common chemical substances. We used a randomly selected sample of 1582 respondents from the Atlanta, Ga, standard metropolitan statistical area. We found that 12.6% of our sample reported the hypersensitivity and that, while the hypersensitivity is more common in women, it is experienced by both men and women of a variety of ages and educational levels. Our prevalence for MCS is similar to that (15.9%) found by the California Department of Health Services in California and suggests that the national prevalence may be similar
- (31) Shannon M, Woolf A, Goldman R. Children's environmental health: one year in a pediatric environmental health specialty unit. *Ambul Pediatr*. 2003;3:53-56.
Abstract: BACKGROUND/OBJECTIVE: As a result of an increasing desire among physicians and parents for clinical centers that can evaluate children with known or suspected exposures to environmental toxicants, a network of federally funded "pediatric environmental health specialty units" has recently been created. This descriptive study profiles the children seen in one unit of this program. SETTING: A New England, university-affiliated Pediatric Environmental Health Center (PEHC). METHODS: Review and analysis of all children seen in the PEHC in calendar year 1999. RESULTS: Over the course of the year, 281 children made 863 visits to the PEHC. Presenting complaints fell into 4 major categories: new visit for management of lead intoxication (n = 248), return visit for management of lead intoxication (n = 569), new visit for evaluation of exposure to an environmental toxicant other than lead (n = 33), and return visit for the management of exposure to a non-lead toxicant (n = 13). Among those children with new visits for a non-lead toxicant, the most common chief complaints were exposure to solvent-contaminated water (n = 7), pesticide exposure (n = 6), illness associated with proximity to a hazardous waste site (n = 6), autism from suspected mercury intoxication (n = 4), and evaluation of school-induced, building-related illness ("sick school syndrome")(n = 4). Eleven children had autism or pervasive developmental delay. Families traveled distances as great as 450 kilometers for evaluation by a pediatric environmental health clinical specialist. Every child was evaluated by a pediatrician with subspecialty training in medical toxicology. Environmental investigation of air, water, paint, dust, or land was conducted for all except 4 children (all foreign-born adoptees). Therapeutic interventions included chelation therapy, relocation to a safe environment, removal from school, and termination of chelation therapy that had been initiated by another practitioner. Third-party payors provided full reimbursement for all visits. CONCLUSIONS: The chief complaints of the children brought to pediatric environmental health specialty units are diverse, involving exposures to a wide range of toxicants from all environmental media (air, water, soil, and food). Parents desiring such an evaluation must often travel extensive distances, suggesting the need for a broader network of

such centers. Third-party payors and health maintenance organizations are willing to provide full reimbursement for these services

- (32) Woolf A. A 4-year-old girl with manifestations of multiple chemical sensitivities. *Environ Health Perspect.* 2000;108:1219-1223.
Abstract: Multiple chemical sensitivities (MCS) syndrome, also known as idiopathic environmental intolerance, is a controversial diagnosis that encompasses a wide range of waxing and waning, subjective symptoms referable to more than one body system and provoked by exposure to low levels of chemicals, foods, or other agents in the environment. Although MCS has been studied extensively, a unifying mechanism explaining the illness remains obscure, and clinicians are divided as to whether such a medical entity exists separately from psychosomatic syndromes. MCS is an adult diagnosis; there is little reference to pediatric cases in the scientific literature. In this case from the Pediatric Environmental Health Subspecialty Unit at Boston's Children's Hospital, I present the case of a preschool child who had suffered from milk allergy and poor weight gain as an infant, and then later developed asthma, allergic symptoms, sinusitis, headaches, fatigue, and rashes precipitated by an expanding variety of chemicals, foods, and allergens. I review definitions, mechanisms, diagnostic strategies, and management, and discuss some uniquely pediatric features of MCS as illustrated by this case
- (33) Bornehag CG, Sundell J, Hagerhed-Engman L, Sigsggard T, Janson S, Aberg N. 'Dampness' at home and its association with airway, nose, and skin symptoms among 10,851 preschool children in Sweden: a cross-sectional study. *Indoor Air.* 2005;15:48-55.
Abstract: Abstract There is convincing epidemiological evidence that 'dampness' in buildings is associated with respiratory effects. In order to identify health-relevant exposures in buildings with 'dampness', the study 'Dampness in Buildings and Health' (DBH) was initiated. In the first step of the study, cross-sectional data on home characteristics including 'dampness' problems, and symptoms in airway, nose, and skin among 10,851 children (1-6 years), were collected by means of a questionnaire to the parents. The prevalence of wheezing during the last 12 months was 18.9% and doctor-diagnosed asthma 5.4%. Rhinitis during the last 12 months was reported for 11.1% of the children and eczema during the last 12 months 18.7%. Gender, allergic symptoms among parents, and age of the child were associated with symptoms. Water leakage was reported in 17.8% of the buildings, condensation on windows in 14.3%, and detached flooring materials in 8.3%. Visible mould or damp spots were reported in only 1.5% of the buildings. The four 'dampness' indices were associated to higher prevalence of symptoms in both crude and adjusted analysis. Furthermore, it was found that the combination of water leakage in the home and PVC as flooring material in the child's or parent's bedroom was associated to higher prevalence of symptoms among children. However, the interpretation of this finding is unclear. The combination of water leakage and PVC may be a proxy, for example, reconstruction because of water damages. Practical Implications The study have showed that moisture-related problems in buildings are a risk factor for asthma and allergic symptoms among preschool children. The recommendation to the general public is to remediate damp buildings
- (34) Savilahti R, Uitti J, Laippala P, Husman T, Roto P. Respiratory morbidity among children following renovation of a water-damaged school. *Arch Environ Health.* 2000;55:405-410.
Abstract: The authors sought to determine whether exposure to molds, resulting from moisture damage in a school, was associated with increased respiratory symptoms and morbidity among schoolchildren and whether the renovation of this building resulted in a decrease in prevalence of respiratory symptoms and morbidity. The study was a follow-up (1-y interval) of children

between the ages of 7 and 12 y from two elementary schools in a Finnish suburb. In addition to a questionnaire completed by the parents, the authors assessed the respiratory health of children by examining the health records of a local health center. In the cross-sectional study, the prevalence of symptoms and infections were higher in the exposed group, as were visits to a physician and use of antibiotics. The school was renovated, after which all prevalence decreased and no significant differences remained, except for visits to a physician (according to questionnaire responses). Therefore, moisture damage and exposure to molds increased the indoor air problems of schools and affected the respiratory health of children

- (35) Guillette EA. A broad-based evaluation of pesticide-exposed children. *Cent Eur J Public Health*. 2000;8 Suppl:58-9.:58-59.

Abstract: Research tends to center on the individual exposed to endocrine disruptors, frequently using a disease centered medical model for evaluative purposes. Pesticides, like many other contaminants, disrupt the endocrine system. A normative growth and developmental model was used to evaluate four- and five-year-old Mexican children living in agricultural areas relying on the use of pesticides and compared the children to those living in a non-agricultural community. The purpose was to determine if the children of any given community were at risk from exposure, in contrast to identifying specific children with multiple deficits. Anthropological methods were adapted to provide a rapid community assessment approach. Living conditions, social and cultural conditions and genetics were similar in all groups studied. Growth, in terms of height and weight were alike for children in both areas. Differences existed in developmental skills, as measured through play behaviors. Neuro-muscular deficits, in terms of coordination and stamina, were found with the children in the agricultural communities. The heavier exposed children also exhibited neuro-mental deficits, as measured through the use of drawing and memory problems. No child excelled or performed poorly on all activities. One important outcome of the study was that behavior standards designed for American children did not always apply to these children due to different expectations placed on the child. Future research needs to examine if other endocrine disrupting compounds create similar developmental deficits

- (36) Meklin T, Potus T, Pekkanen J, Hyvarinen A, Hirvonen MR, Nevalainen A. Effects of moisture-damage repairs on microbial exposure and symptoms in schoolchildren. *Indoor Air*. 2005;15 Suppl 10:40-7.:40-47.

Abstract: Effects of renovation on symptom prevalence and microbial status were studied in two moisture-damaged schools and in two non-damaged schools with longitudinal cross-sectional surveys before and after repairs. Over 1300 schoolchildren aged 6-17 returned questionnaires before and after repairs. After full renovation in one of the damaged schools, elevated concentrations and increased frequencies of indoor air fungi normalized and a significant decrease in the prevalence of 10 symptoms of 12 studied was observed among schoolchildren. No change in microbial conditions was seen after partial repairs in the other damaged school, and only slight improvement was observed in symptom prevalence. The change in the prevalence of symptoms in the reference schools was minor. The results suggest that increased symptom prevalence among schoolchildren in moisture-damaged schools can be managed with proper repair of the moisture damage. PRACTICAL IMPLICATIONS: This longitudinal intervention study showed the positive effects of the moisture and mold damage repairs of a school building on children's health. The success necessitates however, a thorough renovation including appropriate ventilation. Monitoring of airborne viable microbes revealed the damage status of the building and thus could be used as a tool in evaluating the quality of repairs

- (37) Menzies IC. Disturbed children: the role of food and chemical sensitivities. *Nutr Health*. 1984;3:39-54.

Abstract: A wide range of longlasting patterns of symptoms may result from individual sensitivity to substances in the environment such as foods, chemicals, dusts and pollens. Behaviourally disturbed and learning disordered children are common. Their numbers may be increasing and certainly they make great demands on parental understanding and courage as well as on professional judgement and time. A number of case studies are presented which suggest that the difficulties encountered by a significant number of these children have much to do with idiosyncratic responses to foods and additives. This hypothesis requires careful research study at an early date for if validated it will have far reaching implications for the assessment and management of disturbed, delinquent and learning disordered children. Perhaps not enough attention has been paid to the role of biological and environmental factors in the development of children's problems. Certainly recent research has begun to provide support for the concept of environmental (ecologic) illness

- (38) Grandjean P, Harari R, Barr DB, Debes F. Pesticide exposure and stunting as independent predictors of neurobehavioral deficits in Ecuadorian school children. *Pediatrics*. 2006;117:e546-e556.

Abstract: OBJECTIVES: To examine possible effects on blood pressure, neurological function, and neurobehavioral tests in school-aged children with and without prenatal pesticide exposure in an area where stunting is common. METHODS: In a community of Northern Ecuador with intensive floriculture and a high female employment rate, we invited 79 children attending the 2 lowest grades of a public school for clinical examinations. In addition to a thorough physical examination, we administered simple reaction time, Santa Ana dexterity test, Stanford-Binet copying, and Wechsler Intelligence Scale for Children-Revised Digit Spans forward. Maternal interview included detailed assessment of occupational history to determine pesticide exposure during pregnancy. Recent and current pesticide exposure was assessed by erythrocyte acetylcholine esterase activity and urinary excretion of organophosphate metabolites. RESULTS: All eligible children participated in the study, but 7 children were excluded from data analysis due to other disease or age >9 years. A total of 31 of the remaining 72 children were classified as stunted based on their height for age. Maternal occupational history revealed that 37 children had been exposed to pesticides during development. After confounder adjustment, prenatal pesticide exposure was associated with a higher systolic blood pressure than in the controls. On neurological examination, 14 exposed children and 9 controls showed > or =1 abnormalities. Of 5 neurobehavioral tests, the Stanford-Binet copying test showed a lower drawing score for copying designs in exposed children than in controls. Stunting was associated with a lower score on this test only, and both risk factors remained statistically significant in a multiple regression analysis with adjustment for demographic and social confounders. Increased excretion of dimethyl and diethyl metabolites of organophosphates was associated with increased reaction time and no other outcomes. CONCLUSION: Prenatal pesticide exposure may cause lasting neurotoxic damage and add to the adverse effects of malnutrition in developing countries. The effects differ from those due to acute pesticide exposure

- (39) Grandjean P, Landrigan JP. Developmental neurotoxicity of industrial chemicals. *The Lancet*. 2006;DOI:10.1016/S0140-6736(06)69665-7.

Abstract: Neurodevelopmental disorders such as autism, attention deficit disorder, mental retardation, and cerebral palsy are common, costly, and can cause lifelong disability. Their causes are mostly unknown. A few industrial chemicals (eg, lead, methylmercury, polychlorinated biphenyls [PCBs], arsenic, and toluene) are recognised causes of

neurodevelopmental disorders and subclinical brain dysfunction. Exposure to these chemicals during early fetal development can cause brain injury at doses much lower than those affecting adult brain function. Recognition of these risks has led to evidence-based programmes of prevention, such as elimination of lead additives in petrol. Although these prevention campaigns are highly successful, most were initiated only after substantial delays. Another 200 chemicals are known to cause clinical neurotoxic effects in adults. Despite an absence of systematic testing, many additional chemicals have been shown to be neurotoxic in laboratory models. The toxic effects of such chemicals in the developing human brain are not known and they are not regulated to protect children. The two main impediments to prevention of neurodevelopmental deficits of chemical origin are the great gaps in testing chemicals for developmental neurotoxicity and the high level of proof required for regulation. New, precautionary approaches that recognise the unique vulnerability of the developing brain are needed for testing and control of chemicals.

- (40) Bell IR, Schwartz GE, Peterson JM, Amend D. Self-reported illness from chemical odors in young adults without clinical syndromes or occupational exposures. *Arch Environ Health*. 1993;48:6-13.

Abstract: The present survey of young adult college students investigated the prevalence of self-reported illness from the smell of the five following common environmental chemicals (cacosmia): (1) pesticide, (2) automobile exhaust, (3) paint, (4) new carpet, and (5) perfume. Sixty-six percent of 643 students reported feeling ill from one or more of the five chemicals; 15% identified the smell of at least four chemicals as making them ill. Ratings of illness from pesticide correlated weakly but significantly with ratings for the largest number of individual symptoms (9 of 11); daytime tiredness and daytime grogginess both correlated at high levels of significance with illness ratings (on a 5-point scale) for four of the five chemicals. The most cacosmic group (CS) included significantly more women (79%) than the noncacosmic group (NS) (49%); women overall were more cacosmic than men ($p < .001$), even with the significant covariate of depression. Ratings of cacosmia correlated only weakly with scores for depression ($r = 0.16$), anxiety ($r = 0.08$), and trait shyness ($r = 0.18$) in the total sample. On stepwise multiple regression with cacosmia score as the dependent measure, shyness accounted for 5.8% of the variance, while depression, anxiety, sense of mastery, and repression did not enter the equation. Histories of physician-diagnosed hay fever, but not asthma, were more frequent in the CS (16%) than in the NS group (5%). Without the confounds of chronic illness or specific treatment programs, these data are similar to patterns described clinically for a subset of patients with multiple chemical sensitivities (MCS), including previous data on increased nasal resistance in MCS.(ABSTRACT TRUNCATED AT 250 WORDS)

- (41) Huss A, Roosli M. Consultations in primary care for symptoms attributed to electromagnetic fields--a survey among general practitioners. *BMC Public Health*. 2006;6:267.:267.

Abstract: BACKGROUND: Five percent of the Swiss population attribute symptoms to electromagnetic fields (EMF). General practitioners (GPs) might play a key role in recognising an emerging health risk, since they are the first to observe and follow up persons who attribute symptoms to EMF. It is unclear to what extent EMFs have become an issue in general practice and which experiences GPs report from the consultations. METHODS: We conducted telephone interviews in a random sample of GPs in Switzerland in order to assess the frequency of consultations in primary care due to EMF and the GPs' experience with these patients. RESULTS: 342 general practitioners were interviewed, corresponding to a response rate of 28.2%. 69% of the GPs reported at least one consultation due to EMF, but GPs with a certificate in complementary medicine were much more likely to report EMF consultations. The median of

EMF consultation numbers within one year was three. An overview of the most recent EMF-related consultation per GP yielded sleep disorders, headaches and fatigue as the most often reported symptoms and mobile phone base stations, power lines and the own use of mobile phones as the main EMF sources suspected to be associated to symptoms. GPs judged the association between EMF and the symptoms to be plausible in 54% of the cases. There was no combination of symptoms and EMF sources that was remarkably and consistently judged to be a plausible cause of the symptoms. CONCLUSION: In our survey, GPs often judged the association between the health problems and the suspected exposure to be plausible. This plausibility assessment seems to be based on grounds of preventive positions in a situation of scientific uncertainty. More research effort is needed to obtain more insight on a potential association between long term EMF exposure and unspecific symptoms

- (42) Mild KH, Repacholi M, van Deventer E, and Ravazzani P. Proceedings, International Workshop on EMF Hypersensitivity, Prague, Czech Republic, October 25-27, 2004. 2006. http://www.who.int/peh-emf/publications/reports/EHS_Proceedings_June2006.pdf
Abstract: A WHO workshop on Electromagnetic Hypersensitivity was held in Prague on October 25-27, 2004. This meeting was arranged in collaboration with the National Reference Laboratory for Non-Ionizing Radiation, Ministry of Health, Czech Republic and was cosponsored by the European Commission Coordinated Action EMF-NET and the Action COST 281 (Potential Health Implications from Mobile Communication Systems) within the European Framework for Cooperation in the Field of Scientific and Technical Research. Sensitivity to EMF has been given the general name "Electromagnetic Hypersensitivity" or EHS. It comprises nervous system symptoms like headache, fatigue, stress, sleep disturbances, skin symptoms like prickling, burning sensations and rashes, pain and ache in muscles and many other health problems. Whatever its cause, EHS is a real and sometimes a disabling problem for the affected persons. Their EMF exposure is generally several orders of magnitude under the limits of internationally accepted standards. The aim of the conference was to review the current state of knowledge and opinions of the conference participants and propose ways forward on this issue.
- (43) International Commission for Electromagnetic Safety (ICEMS). Benevento Resolution. International Commission for Electromagnetic Safety (ICEMS) . 2006. www.milieuziektes.nl/Rapporten/BeneventoResolution.pdf
Abstract: We, the undersigned scientists, agree to assist in the promotion of EMF research and the development of strategies to protect public health through the wise application of the precautionary principle.
Precautionary strategies should be based on design and performance standards and may not necessarily define numerical thresholds because such thresholds may erroneously be interpreted as levels below which no adverse effect can occur. These strategies should include:
- 6.1. Promote alternatives to wireless communication systems, e.g., use of fiber optics and coaxial cables; design cellular phones that meet safer performance specifications, including radiating away from the head; preserve existing land line phone networks; place power lines underground in the vicinity of populated areas, only siting them in residential neighborhoods as a last resort;
 - 6.2. Inform the population of the potential risks of cell phone and cordless phone use. Advise consumers to limit wireless calls and use a land line for long conversations.
 - 6.3. Limit cell phone and cordless phone use by young children and teenagers to the lowest possible level and urgently ban telecom companies from marketing to them.
 - 6.4. Require manufacturers to supply hands-free kits (via speaker phones or ear phones), with

each cell phone and cordless phone.

6.5. Protect workers from EMF generating equipment, through access restrictions and EMF shielding of both individuals and physical structures.

6.6. Plan communications antenna and tower locations to minimize human exposure. Register mobile phone base stations with local planning agencies and use computer mapping technology to inform the public on possible exposures. Proposals for city-wide wireless access systems (e.g. Wi-Fi, WIMAX, broadband over cable or power-line or equivalent technologies) should require public review of potential EMF exposure and, if installed, municipalities should ensure this information is available to all and updated on a timely basis.

6.7. Designate wireless-free zones in cities, in public buildings (schools, hospitals, residential areas) and, on public transit, to permit access by persons who are hypersensitive to EMF.

- (44) European Parliament Press Service. Parliament adopts REACH - new EU chemicals legislation and new chemicals agency. *Exp.Biol.Med.*(Maywood.). 13-12-2006. available from http://www.europarl.europa.eu/news/expert/infopress_page/064-1496-345-12-50-911-20061213IPR01493-11-12-2006-2006-true/default_en.htm

Abstract: Parliament adopted the compromise it negotiated with Council on the new regulation for chemicals, REACH, which will oblige producers to register all those chemical substances produced or imported above a total quantity of 1 tonne per year. Registration will affect about 30,000 substances. For more hazardous substances, producers will have to submit a substitution plan to replace them with safer alternatives.

When no alternative exists, producers will have to present a research plan aimed at finding one. The compromise package agreed with the Council and tabled by 4 political groups (EPP-ED, PES, ALDE and UEN), was approved with 529 in favour, 98 against and 24 abstentions.

- (45) Seidel HJ. Environmental medicine in Germany--a review. *Environ Health Perspect.* 2002;110 Suppl 1:113-8.:113-118.

Abstract: In this review I describe the development of environmental medicine as a specialized field of clinical medicine in Germany. New scientific societies were founded, based on traditions of public hygiene and occupational medicine, as a reaction to environmental issues concerning human health. Environmental medicine issues were also addressed by independent "critical" physicians. The first institutions to accept patients were centers for environmental medicine affiliated with research institutions and/or with the public health service. Medical professional organizations, particularly the German General Medical Council, described the need for and formulated conditions for additional qualification for doctors in environmental medicine, including a 200-hr course. This course and a qualifying exam were passed by about 3,000 doctors, mainly from the public health service and from occupational medicine.

Unfortunately, few general physicians in primary outpatient care were similarly trained. To date, no representative study has been conducted on environmental patients, but I include in this review a typical list of patients' complaints. I also summarize research activities typical for environmental medicine in Germany. Present problems concern accounting systems and, for example, diagnosis and treatment of patients with multiple chemical sensitivities (MCS). A coordinated research program on MCS has been started

- (46) Danish Environmental Protection Agency and Danish Ministry of the Environment. Multiple Chemical Sensitivity, MCS, Environmental Project no. 988, 2005. Danish Environmental Protection Agency . 2005. available from http://www.mst.dk/homepage/default.asp?Sub=http://www.mst.dk/udgiv/publications/2005/87-7614-548-4/html/helepubl_eng.htm

Abstract: Based on the information of this report the following attempts are indicated for reducing exposure to chemicals:

- Generally, limited use of chemicals in everyday life
- Limited use of volatile chemicals (e.g. scents) and chemicals in the form of aerosols for personal and household use.
- Limited use of pesticides and biocides.

Special attention might be directed towards:

- Cosmetics, cleaning products and products for surface treatment regarding their use and content, and
- In-door air pollution from building materials and furniture as well as tobacco smoke and exhausts from traffic.

Preventive action for MCS could contribute to a better protection of all those exposed to chemicals, especially the most vulnerable groups. Recognition of the illness MCS would lead to a better understanding of MCS patients and their needs.

- (47) World Health Organization. History of the development of the ICD. World Health Organization . 2006. <http://www.who.int/classifications/icd/en/HistoryOfICD.pdf>
- (48) World Health Organization. Cumulative Official Updates to ICD-10. World Health Organization . 2006. <http://www.who.int/classifications/committees/ICDCombinedUpdates.pdf> available from <http://www.who.int/classifications/icd/icd10updates/en/index.html>
- (49) Canadian Institute for Health Information. International Statistical Classification of Diseases and Related Health Problems. Canadian Institute for Health Information . 2006. secure.cihi.ca/cihiweb/en/downloads/ICD-10-CA_Vol2_2006.pdf
- (50) Health Canada. Environmental Sensitivities - Drugs and Health Products Newsletter. Health Canada . 2005. available from http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/bulletin/tpd_dpt_bulletin02_2005_e.html
Abstract: More and more people report having adverse reactions to common substances in their daily environment. Products such as perfumes, air fresheners, hairsprays or aftershave lotions can trigger, in some people, reactions ranging from mild to serious.
Reported common reactions of sensitivities may include: wheezing, shortness of breath, headaches, sore throat, eye irritation, nausea, sinus pain, dizziness, fatigue, poor concentration, anxiety, sweating, joint aches, and skin irritation.
What can you do?
* Be aware of employees' sensitivities.
* Avoid wearing perfume, aftershave, scented personal toiletries, hair spray and gel.
* Refrain from bringing flowering plants, cut flowers and air fresheners into the workplace.
* If you have allergies or sensitivities, politely let others around you know of your health concerns.
* If you are aware of someone who is sensitive, be considerate and avoid using the substances which might trigger a negative reaction.
- (51) Canadian Health Network. What is chemical sensitivity? Canadian Health Network. Canadian Public Health Agency . 2006. available from <http://www.canadian-health-network.ca/servlet/ContentServer?cid=1003484&pagename=CHN-RCS%2FCHNResource%2FFAQCHNResourceTemplate&c=CHNResource&lang=En>

- (52) Pest Management Regulatory Agency, Health Canada. Proposed Acceptability for Continuing Registration. Re-evaluation of Malathion. PACR2003-10. Pest Management Regulatory Agency, Health Canada. 2003. <http://www.pmra-arla.gc.ca/english/pdf/pacr/pacr2003-10-e.pdf>
Abstract: Bystander risk estimates are above the target MOE for all exposure routes and scenarios associated with either ground ULV or aerial ULV applications. The MOEs that were attained were sufficiently large and thus are anticipated to provide further accommodation for those with environmental sensitivities. The MOEs would be further enhanced through measures such as remaining indoors during and immediately after spraying. Following non-ULV ground application at higher rates, unacceptable MOEs are obtained for inhalation exposures for adolescents and toddlers.
- (53) Sears M, Walker CR, van der Jagt RHC, Claman P. Pesticide Assessment: Protecting Public Health on the Home Turf. *Paediatr Child Health*. 2006;11:229-234.
Abstract: Pesticide regulation is examined in the context of Health Canada's Pest Management Regulatory Agency's assessment of the chlorophenoxy herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) for turf. 2,4-D is the most common herbicide used to kill weeds in grass. The medical literature does not uniformly indicate harms from herbicides. However, the balance of epidemiological research suggests that 2,4-D can be persuasively linked to cancers, neurological impairment and reproductive problems. These may arise from 2,4-D itself, from breakdown products or dioxin contamination, or from a combination of chemicals. Regulators rely largely on toxicology, but experiments may not replicate exposures from 2,4 D application to lawns because environmental breakdown products (eg, 2,4-dichlorophenol) may not accumulate and selected herbicides are possibly less contaminated. Dioxins are bioaccumulative chemicals that may cause cancer, harm neurological development, impair reproduction, disrupt the endocrine system and alter immune function. No dioxin analyses were submitted to the Pest Management Regulatory Agency, and the principal contaminants of 2,4-D are not among the 17 congeners covered in pesticide regulation. Independent assessment of all dioxins is needed, in tissues and in the environment. The 2,4-D assessment does not approach standards for ethics, rigour or transparency in medical research. Canada needs a stronger regulator for pesticides. Potentially toxic chemicals should not be registered when more benign solutions exist, risks are not clearly quantifiable or potential risks outweigh benefits. Until landscaping pesticides are curtailed nationally, local bylaws and Quebec's Pesticide Code are prudent measures to protect public health. Physicians have a role in public education regarding pesticides.
- (54) Canadian Centre for Occupational Health and Safety. Indoor Air Quality: A Legitimate OSH Concern. Canadian Centre for Occupational Health and Safety . 2006. available from <http://www.ccohs.ca/headlines/text27.html>
Abstract: IAQ is a suspect when building occupants experience one or several of the following symptoms: headaches, fatigue, shortness of breath, sinus congestion, coughing, sneezing, dizziness, nausea, and irritation to the skin, eyes, nose and throat. These symptoms can usually be attributed to inadequate temperature, lack of humidity or lighting; exposure to chemicals, dusts, gases, vapours and odours; or a lack of fresh air from the ventilation system. People generally develop symptoms within a few hours of starting the workday and feel better after leaving the building. Collectively, these symptoms are often referred to as "Sick Building Syndrome."The reason IAQ problems are difficult to determine is that building occupants are exposed to not one but several adverse conditions. For example, you might not think that the slight emissions from furniture, carpets, photocopiers, or the perfume worn by your co-workers could be harmful, but in combination they can affect your health. Again, these effects are

impossible to trace accurately, but the condition does have a name: Multiple Chemical Sensitivity (MCS).

- (55) Byus CM, Glickman BW, Krewski D, Lotz GW, Mandeville R, McBride ML, Prato FS, and Weaver DF. A review of the Potential Health Risks of Radiofrequency Fields from Wireless Telecommunication Devices. 1999. Royal Society of Canada, for Health Canada. http://www.rsc.ca/files/publications/expert_panels/RF/RFreport-en.pdf available from http://www.rsc.ca/index.php?lang_id=1&page_id=120
Abstract: Based on its review of the currently available scientific literature, the panel recommends that further research into the potential health effects of radiofrequency fields be conducted, particularly in the area of non-thermal effects. This research will require the collaborative efforts of researchers with expertise in a number of diverse areas, including engineering, radiation dosimetry and the biological and health sciences. The committee identified four distinct scientific approaches to further our knowledge of RF fields. In vivo and in vitro laboratory experiments conducted at both the cellular and animal level can be used to obtain information on the potential adverse health effects of radiofrequency fields using nonhuman test systems. Molecular studies provide an opportunity to elucidate the mechanisms by which biological effects occur at non-thermal exposure levels, thereby providing a basis for evaluating the significance of such biological effects. Clinical studies may be particularly useful in identifying susceptible population subgroups. Epidemiological studies are needed to monitor the potential health effects of long term exposure to radiofrequency fields.
- (56) Krewski D, Byus CV, Glickman BW, Habash RWY, Habbick B, Lotz GW, Mandeville R, McBride ML, Prato FS, Salem T, and Weaver DF. Recent Advances in Research on Radiofrequency Fields and Health: 2001-2003
A Follow-up to The Royal Society of Canada Report on the Potential Health Risks of Radiofrequency Fields from Wireless Telecommunication Devices, 1999 and update. Royal Society of Canada . 2004. http://www.rsc.ca/files/publications/expert_panels/RF//expert_panel_radiofrequency_update2.pdf
Abstract: The widespread use of wireless telecommunications devices, particularly mobile phones, has resulted in increased human exposure to radiofrequency (RF) fields. Although national and international agencies have established safety guidelines for exposure to RF fields, concerns remain about the potential for adverse health outcomes to occur in relation to RF field exposure. The extensive literature on RF fields and health has been reviewed by a number of authorities, including the Royal Society of Canada (1999), the American Cancer Society (2001), the European Commission's Scientific Committee on Toxicity, Ecotoxicity and the Environment (2001), the British Medical Association (2001), the Swedish Radiation Protection Authority (2002), and the Health Council of the Netherlands (2002). This report provides an update on recent research results on the potential health risks of RF fields since the publication of the Royal Society of Canada report in 1999 (J. Toxicol. Env. Heal., B4, 1-143) and our previous 2001 update (J. Toxicol. Env. Heal., B4, 145-149), covering the period 2001-2003. The present report examines new data on dosimetry and exposure assessment, thermoregulation, biological effects such as enzyme induction, and toxicological effects, including genotoxicity, carcinogenicity, and testicular and reproductive outcomes. Epidemiological studies of mobile phone users and occupationally exposed populations are examined, along with human and animal studies of neurological and behavioural effects. All of the authoritative reviews completed within the last two years have concluded that there is no clear evidence of adverse health effects associated with RF fields. At the same time, these same

reviews support the need for further research to clarify the possible associations between RF fields and adverse health outcomes that have appeared in some reports. The results of the ongoing WHO study of mobile phones will provide important new information in this regard.

- (57) Cunningham R. National and Subnational Legislation Requiring Enclosed Restaurants and Bars to be 100% Smoke-free. Ottawa Council on Smoking and Health . 20-7-2006.
<http://www.smokefreeottawa.com/2006-en/pdfs/smokefreevacations.pdf> available from
<http://www.smokefreeottawa.com/2006-en/health-3.shtml>
Abstract: Canadian provinces/territories (9 of 13)
1. Northwest Territories (May 1, 2004)
2. Nunavut Territory (May 1, 2004)
3. New Brunswick (Oct. 1, 2004)
4. Manitoba (Oct. 1, 2004)
5. Saskatchewan (Jan. 1, 2005)
6. Newfoundland and Labrador (July 1, 2005)
7. Ontario (May 31, 2006)
8. Quebec (May 31, 2006)
9. Nova Scotia (Dec. 1, 2006) *
* legislation also applies to all of (or most of) any outdoor premises of restaurants and bars
- (58) Développement durable, Environnement et Parcs Québec. The Pesticides Management Code. Québec - Développement durable, Environnement et Parcs . 2006. available from
<http://www.mddep.gouv.qc.ca/pesticides/permis-en/code-gestion-en/index.htm>
Abstract: The Pesticides Management Code, in force since April 3, 2003, sets strict standards to control the use and sale of pesticides. This new regulation aims at limiting the harmful effects of pesticides on human health – especially on the health of children – and on the environment. The environmental management approach that it advocates limits the non-essential use of pesticides to the bare essentials in matters of lawn maintenance. Childcare centres, elementary and secondary schools have to be as free as possible from pesticides.
- (59) Santé et Services sociaux Québec. Plan d'intervention de protection de la santé publique contre le virus du Nil occidental 2006. Gouvernement du Québec, 2006 . 2006.
<http://intranetreseau.rtss.qc.ca> et www.msss.gouv.qc.ca
Abstract: La philosophie du plan d'intervention préconise le respect de la législation existante en matière de lutte contre le VNO et prévoit l'utilisation de toutes les possibilités telles que les mesures de protection personnelle, domestique, communautaire et municipale. Toutefois, si une situation atteignait un niveau extrême, difficilement contrôlable en présence de plusieurs cas humains regroupés, l'application d'insecticides à des fins sanitaires pourrait être envisagée. Un programme de surveillance des cas humains et des moustiques vecteurs infectés par le VNO a été mis en place afin d'assurer un suivi de la situation. Le plan d'intervention prévoit que, en cas de situation épidémique, des actions possibles seront évaluées par un comité avisé à composition intersectorielle soutenu par un groupe d'experts. Ce comité fera, aux autorités décisionnelles, ses recommandations sur les interventions optimales contre le VNO.
- (60) Thomson GM, Day JH, Ewers SE, Gerrard JW, McCourtie DR, and Woodward WD. Report of the ad hoc committee on environmental sensitivities. 1985.
- (61) Jones D. Nova Scotia only province to provide clinic for "environmentally sensitive" patients. *CMAJ*. 1992;147:931-933.

- (62) WorkSafeBC Policy and Research Division. Compensation for Occupational Asthma and Contact Dermatitis Policy and Research Division Discussion Paper. Ontario Workplace Tribunals Library [owtlibrary.on.ca](http://www.owtlibrary.on.ca) . 2006. http://www.owtlibrary.on.ca/Catalogued_PDF/ED%20284.pdf
 Abstract: A worker who develops an allergy or hypersensitivity to a workplace substance that results in an asthmatic reaction or signs and symptoms of contact dermatitis is considered to have an occupational disease. Compensation is payable to such a worker during the period he or she is symptomatic. Under current policy, compensation, in the form of wage loss and/or a permanent disability award, is not payable when the worker's signs and symptoms have resolved and he or she is simply left with an underlying allergy or hypersensitivity to the workplace substance.
 At issue is whether, given current scientific evidence, policy should be amended to provide compensation to workers who are asymptomatic¹ when removed from work, but who must avoid worksites containing a triggering substance or risk increasingly severe asthmatic reactions or flare-ups of contact dermatitis.
- (63) Christie M. Private Property Pesticide By-laws In Canada Population Statistics by Municipality. www.healthyottawa.ca . 2006. <http://www.flora.org/healthyottawa/BylawList.pdf> available from <http://www.flora.org/healthyottawa/BylawList.pdf>
 Abstract: The lack of adequate protection from unwanted exposure to lawn pesticides at the federal and provincial level has fueled a growing surge in municipal pesticide restrictions designed to enhance the protection of the environment and public health. The number of municipal by-laws currently in place across Canada has now increased to 124. An additional 7 pesticide by-laws are at the draft stage pending adoption. Municipalities of all sizes have passed various forms of pesticide by-laws. The largest is the City of Toronto with a population of 2.48 million while some are as small as Lac- Saint-Joseph, Québec with a population of 184. There are over 12 million Canadians, or 38% of Canada's total population (based on 2001 Census) benefiting from enhanced protection from unwanted exposure to synthetic lawn and garden pesticides. This figure includes the additional province-wide protection provided under Québec's Pesticide Management Code. There are 1141 municipalities (cities, villages and townships in Québec.
- (64) Canadian Medical Association. Policy resolution GC04-50 - Combined fertilizer / pesticides. 18-8-2004. available from http://policybase.cma.ca/dbtw-wpd/exec/dbtwpub.dll?AC=GET_RECORD&XC=/dbtw-wpd/exec/dbtwpub.dll&BU=http%3A%2F%2Fpolicybase.cma.ca%2Fdbtw-wpd%2FCMAPolicy%2FPublicB.htm&TN=PubPol&SN=AUTO15679&SE=3096&RN=0&MR=20&TR=0&TX=1000&ES=0&CS=1&XP=&RF=Public%3E+TableDE&EF=&DF=Public%3E+DetailE&RL=0&EL=0&DL=0&NP=3&ID=&MF=wpengmsgcmapolicypublicB.ini&MQ=&TI=0&DT=&ST=0&IR=680&NR=0&NB=0&SV=0&BG=0&FG=000000&QS=Staff
 Abstract: Text of Policy resolution: The Canadian Medical Association calls on the federal government to rescind the registration of combined fertilizer/pesticides.
- (65) Marshall L, Weir E, Abelsohn A, Sanborn MD. Identifying and managing adverse environmental health effects: 1. Taking an exposure history. *CMAJ*. 2002;166:1049-1055.
 Abstract: Public concern and awareness are growing about adverse health effects of exposure to environmental contaminants. Frequently patients present to their physicians with questions or concerns about exposures to such substances as lead, air pollutants and pesticides. Most primary care physicians lack training in and knowledge of the clinical recognition, management and

avoidance of such exposures. We have found that it can be helpful to use the CH2OPD2 mnemonic (Community, Home, Hobbies, Occupation, Personal habits, Diet and Drugs) as a tool to identify a patient's history of exposures to potentially toxic environmental contaminants. In this article we discuss why it is important to take a patient's environmental exposure history, when and how to take the history, and how to interpret the findings. Possible routes of exposure and common sources of potentially toxic biological, physical and chemical substances are identified. A case of sick-building syndrome is used to illustrate the use of the mnemonic

- (66) Robb N. The environment was right for Nova Scotia's new environmental health clinic. *CMAJ*. 1995;152:1292-1295.
Abstract: With a \$1-million contribution from the Nova Scotia government, Dalhousie University medical school is establishing an environmental health clinic that will research and treat the controversial condition known as multiple-chemical sensitivity. Already several hundred Nova Scotians, including about 100 former employees of Halifax's Camp Hill Hospital, have been referred to a part-time clinic that addresses environmental illness and other unexplained conditions. Some physicians contend that the sensitivity is largely psychosomatic and treatments provide little more than a placebo effect, but proponents believe research will support environmental health's goal of becoming a new, recognized speciality
- (67) Rafuse J. Practical application of air-quality research incorporated in CMHC's research house. *CMAJ*. 1995;152:1310-1311.
Abstract: The Canada Mortgage and Housing Corporation has been looking at ways to improve indoor air quality since 1984 and now hopes to interest house designers and manufacturers in the results of its research. Its flagship project has been the construction of a proto-type research house for environmentally hypersensitive people
- (68) Gray C. Waiting list already 7 months long at Toronto's new Environmental Health Clinic. *CMAJ*. 1997;156:879-881.
Abstract: Following the head set by Nova Scotia, Ontario now has a clinic devoted to the treatment of patients with "environmental illness." It opened in Toronto last year, and patients must be referred by their family physician and complete a 16-page previsit questionnaire. They receive a 3-hour assessment in which their medical history is explored, plus a full physical examination and blood and urine tests. Dr. Frank Foley, who heads the Toronto clinic, says his patients have seen from 8 to 10 health care professionals in the 2 years before their visit and most have been told the problem is "in your head." He says they need to "have their symptoms validated and their distress acknowledged."
- (69) Ontario College of Family Physicians. Taking An Exposure History.
<http://www.ocfp.on.ca/english/ocfp/communications/publications/default.asp?s=1> . 2005.
- (70) Miller CS, Prihoda TJ. The Environmental Exposure and Sensitivity Inventory (EESI): a standardized approach for measuring chemical intolerances for research and clinical applications. *Toxicol Ind Health*. 1999;15:370-385.
Abstract: The lack of a generally accepted case definition for multiple chemical sensitivity (MCS) and the absence of a standardized approach for measuring salient aspects of chemical sensitivity that would permit cross-comparison of findings by different investigators have hindered progress in this area. Based upon findings from an earlier study of 112 persons with self-reported chemical sensitivity who attributed their chemical sensitivity to a well-defined exposure event, we developed an instrument with self-rating scales to assess Symptom Severity,

Chemical (Inhalant) Intolerances, Other Intolerances (e.g., foods, medications, alcohol), Life Impact, and Masking (a measure of ongoing chemical exposures). When administered to four patient groups and controls, the scales showed good reliability and validity overall (n = 421) and in each group. Used together, the scales provided sensitivity of 92% and specificity of 95% in differentiating chemically sensitive persons from controls. Our results support use of these scales individually or collectively for a variety of applications including the selection of chemically sensitive subjects and controls for research, assessment of chemical sensitivity in various study populations, cross-comparison of groups studied by different investigators, pre- and post-assessment of therapeutic interventions, clinical evaluation of complex patients who report intolerances, and teaching medical residents and students how to evaluate patients for chemical sensitivity and MCS

- (71) Rea WJ, Didriksen N, Simon TR, Pan Y, Fenyves EJ, Griffiths B. Effects of toxic exposure to molds and mycotoxins in building-related illnesses. *Arch Environ Health*. 2003;58:399-405. Abstract: The authors studied 100 patients who had been exposed to toxic molds in their homes. The predominant molds identified were *Alternaria*, *Cladosporium*, *Aspergillus*, *Penicillium*, *Stachybotrys*, *Curvularia*, *Basidiomycetes*, *Myxomycetes*, smuts, *Epicoccus*, *Fusarium*, *Bipolaris*, and *Rhizopus*. A variety of tests were performed on all, or on subgroups of, these patients. Sensitivities and exposures were confirmed in all patients by intradermal skin testing for individual molds (44-98% positive), and by measurement of serum antibodies. Abnormalities in T and B cells, and subsets, were found in more than 80% of the patients. The findings of trichothecene toxin and breakdown products in the urine, serum antibodies to molds, and positive intradermal skin tests confirmed mycotoxin exposure. Respiratory signs (e.g., rhinorrhea, sinus tenderness, wheezing) were found in 64% of all patients, and physical signs and symptoms of neurological dysfunction (e.g., inability to stand on the toes or to walk a straight line with eyes closed, as well as short-term memory loss) were identified in 70% of all patients. Objective abnormal autonomic nervous system tests were positive in all 100 patients tested. Brain scans, conducted using triple-head single photon emission computed tomography, were abnormal in 26 (86%) of 30 (subgroup of the 100) patients tested. Objective neuropsychological evaluations of 46 of the patients who exhibited symptoms of neurological impairment showed typical abnormalities in short-term memory, executive function/judgment, concentration, and hand/eye coordination
- (72) Joffres MR, Sampalli T, Fox RA. Physiologic and symptomatic responses to low-level substances in individuals with and without chemical sensitivities: a randomized controlled blinded pilot booth study. *Environ Health Perspect*. 2005;113:1178-1183. Abstract: We conducted a pilot study using a randomized, single-blind, placebo-controlled exposure among 10 individuals with and 7 without reported chemical sensitivities in a dedicated testing chamber. Objectives of the study were to explore the length of the adaptation period to obtain stable readings, evaluate responses to different substances, and measure the level and type of symptomatic and physiologic reactions to low-level exposures. Reported and observed symptoms, electrodermal response, heart rate, skin temperature, surface electromyogram, respiratory rate, contrast sensitivity, and the Brown-Peterson cognitive test were used and compared between cases and controls and between test substances (glue, body wash solution, dryer sheet) and control substances (unscented shampoo and clean air). Subjects with chemical sensitivities (cases) took longer to adapt to baseline protocols than did controls. After adaptation, despite small study numbers, cases displayed statistically significant responses (all measures, $p < 0.02$) in tonic electrodermal response to test substances compared with controls and compared with the control substance. Symptoms were also higher in cases than in controls

for the body wash solution ($p = 0.05$) and dryer sheets ($p = 0.02$). Test-retest showed good agreement for both symptoms and tonic electrodermal responses (McNemar's test, $p = 0.32$ and $p = 0.33$, respectively). Outside of skin conductance, other measures had no consistent patterns between test and control substances and between cases and controls. This study shows the importance of using an adaptation period in testing individuals with reported chemical sensitivities and, despite small numbers, raises questions about underlying mechanisms and level of reactivity to low-level chemical exposures in sensitive individuals

- (73) Ashford N, Miller C. *Chemical Exposures Low levels and High Stakes*. 2nd ed. van Nostrand Reinhold. NY. Nelson Canada; 1998.
- (74) Fox RA. The Environment and Multiple Chemical Sensitivity. Nova Scotia Environmental Health Centre, Dalhousie University, Fall River, Nova Scotia, Canada. 2006. Nova Scotia Environmental Health Centre, Dalhousie University, Fall River, Nova Scotia, Canada. <http://www.cdha.nshealth.ca/facilities/nsehc/studyEnvironmentAndES.PDF> available from <http://www.cdha.nshealth.ca/facilities/nsehc/studyEnvironmentAndES.PDF>
Abstract: In a sample of 100 patients who fulfilled the consensus criteria for multiple chemical sensitivity, MCS, 40 had no clear cut event associated with onset of illness. Seventeen had acute onset and attributed this to a single, significant environmental problem. Thirty five attributed onset to various environmental exposures from contaminated ambient air of childhood or adult life, from indoor air at home, from hobbies or from occupation. Eight patients linked acute onset to other events such as a motor vehicle accident, childbirth or viral illness. Thirty four worked in "tight buildings" and 22 reported an indoor air quality problem. If environmentally contaminating, manufactured chemicals are causally linked to the etiology of MCS then exposure is most likely long term and to low, so called "safe levels", of complex mixtures. It is likely that environmental contaminants interact with host factors as part of a causal web.
- (75) Saijo Y, Kishi R, Sata F et al. Symptoms in relation to chemicals and dampness in newly built dwellings. *Int Arch Occup Environ Health*. 2004;77:461-470.
Abstract: OBJECTIVES: As the airtightness of dwellings has recently increased, problems associated with indoor air pollution and dampness have become important environmental health issues. The aim of this study was to clarify whether symptoms in residents living in newly built dwellings were related to chemicals and dampness. METHODS: Symptoms of 317 residents were surveyed by standardized questionnaires, and the concentrations of formaldehyde, acetaldehyde, and 17 volatile organic compounds (VOCs) in their homes were measured. Dampness (condensation on window panes and/or walls, and mold growth) was identified by questionnaires given to the householders or their partners. RESULTS: Some VOCs (toluene, butyl acetate, ethylbenzene, alpha-pinene, p-dichlorobenzene, nonanal, and xylene) were significantly related to the symptoms, and the sum of all VOCs (all identified VOCs) was significantly related to throat and respiratory symptoms [odds ratio (OR) for eye symptoms = 2.4; 95% confidence interval (CI) 1.0-5.5], although the concentrations of VOCs were relatively low. As for the dampness index, condensation on window panes and/or walls was related to all symptoms, and mold growth was related to all symptoms except skin, throat and respiratory and general symptoms. As the number of dampness signs increased, the ORs increased for the symptoms except general symptoms (OR for nose symptoms = 4.4, 95% CI 1.6-11.9). CONCLUSION: Both VOCs and dampness were significantly related to symptoms. We should take measures to reduce the concentrations of VOCs, dampness and microbial growth in dwellings

- (76) Bourbeau J, Brisson C, Allaire S. Prevalence of the sick building syndrome symptoms in office workers before and six months and three years after being exposed to a building with an improved ventilation system. *Occup Environ Med.* 1997;54:49-53.
Abstract: OBJECTIVE: The prevalence of symptoms associated with the sick building syndrome (SBS) has recently been shown to decrease by 40% to 50% among office workers six months after they were exposed to a building with an improved ventilation system. The objective of the present study was to find whether the decrease in the prevalence of symptoms was maintained three years later. METHODS: Workers from the same organisation occupied five buildings in 1991 and moved during that year to a single building with an improved ventilation system. All buildings had sealed windows with mechanical ventilation, air conditioning, and humidification. Workers completed a self administered questionnaire during normal working hours in February 1991 before moving, in February 1992 six months after moving, and in February 1995, three years after moving. The questionnaire encompassed symptoms of the eyes, nose and throat, respiratory system, skin, fatigue, and headache, as well as difficulty concentrating, personal, psychosocial, and workstation factors. During normal office hours of the same weeks, environmental variables were measured. RESULTS: The study population comprised 1390 workers in 1991, 1371 in 1993, and 1359 in 1995, which represents 80% of the population eligible each year. The prevalence of most symptoms decreased by 40% to 50% in 1992 compared with 1991. This was similar in 1995. These findings were significant and remained generally similar after controlling for personal, psychosocial, and work related factors. CONCLUSION: In this study, the decrease of 40% to 50% in the prevalence of most symptoms investigated six months after workers were exposed to a new building with an improved ventilation system was maintained three years later. The results of the present follow up study provide further support for a real effect of exposure to a new building with an improved ventilation system on the prevalence of symptoms associated with the SBS
- (77) Gibson PR, Placek E, Lane J, Brohimer SO, Lovelace AC. Disability-induced identity changes in persons with multiple chemical sensitivity. *Qual Health Res.* 2005;15:502-524.
Abstract: In this qualitative study, the authors asked respondents with multiple chemical sensitivity (MCS) in an open-ended question how having the condition affected their identities. Authors then examined responses for themes, which they discuss within the framework of critical theory. Emergent themes included loss of a stable, familiar personality, loss of self-positioning, emotional suppression to meet others' expectations, redesigning the planned life, forced growth, struggling with support, discovering the spiritual self, and identity reconsolidation. The authors compare findings with published works on adjustment to chronic illness and other delegitimized illnesses, find them to be fairly congruent, and then discuss problems regarding cultural acceptance of MCS as a condition caused by chemical exposure
- (78) Kassirer J and Sandiford K. Socio-Economic Impacts of Environmental Illness in Canada. 15-11-2000. The Environmental Illness Society of Canada.
Abstract: Incidence
- About one in eight (several million) adult Canadians suffer significant symptoms, increased absenteeism, and measurably impaired abilities at work due to 'normally safe' exposures to some of the common chemicals and molds found in their homes and at work.
 - About one in 50 (about half a million) adult Canadians are unable to do paid work due to a disability associated with Environmental Illness.
- Impacts on Society
- Over ten billion dollars a year in lost productivity
 - Over 1 billion each year eroded from the tax base

- Over 1 billion dollars each year in health care costs, much of which could be avoided if the illness were diagnosed and treated in a timely manner
- Over 1 billion dollars each year in avoidable disability payments
- Avoidable costs to private health plans (not measured)
- Avoidable suicides (not measured)
- Erosion of personal rights and universality of healthcare

Impacts on Individuals and their Families

- One million Canadian adults are less productive or underemployed, and are needing to renovate their homes
- Half a million Canadian adults are
 - o unable to do paid work,
 - o isolated,
 - o facing additional costs such as organic foods and uncovered medications, medical services and assistive devices - which can easily total \$10,000 a year, and are
 - o depleting their RRSPs and other savings
- Hundreds of thousands of Canadian adults are relatively homeless, and thousands are absolutely homeless
- Failed marriages and family tension
- Suicide

- (79) Wargocki P, Wyon DP, Sundell J, Clausen G, Fanger PO. The effects of outdoor air supply rate in an office on perceived air quality, sick building syndrome (SBS) symptoms and productivity. *Indoor Air*. 2000;10:222-236.

Abstract: Perceived air quality, Sick Building Syndrome (SBS) symptoms and productivity were studied in a normally furnished office space (108 m³) ventilated with an outdoor airflow of 3, 10 or 30 L/s per person, corresponding to an air change rate of 0.6, 2 or 6 h⁻¹. The temperature of 22 degrees C, the relative humidity of 40% and all other environmental parameters remained unchanged. Five groups of six female subjects were each exposed to the three ventilation rates, one group and one ventilation rate at a time. Each exposure lasted 4.6 h and took place in the afternoon. Subjects were unaware of the intervention and remained thermally neutral by adjusting their clothing. They assessed perceived air quality and SBS symptoms at intervals, and performed simulated normal office work. Increasing ventilation decreased the percentage of subjects dissatisfied with the air quality ($P < 0.002$) and the intensity of odour ($P < 0.02$), and increased the perceived freshness of air ($P < 0.05$). It also decreased the sensation of dryness of mouth and throat ($P < 0.0006$), eased difficulty in thinking clearly ($P < 0.001$) and made subjects feel generally better ($P < 0.0001$). The performance of four simulated office tasks improved monotonically with increasing ventilation rates, and the effect reached formal significance in the case of text-typing ($P < 0.03$). For each two-fold increase in ventilation rate, performance improved on average by 1.7%. This study shows the benefits for health, comfort and productivity of ventilation at rates well above the minimum levels prescribed in existing standards and guidelines. It confirms the results of a previous study in the same office when the indoor air quality was improved by decreasing the pollution load while the ventilation remained unchanged

- (80) Fisk WJ, Rosenfeld AH. Estimates of Improved Productivity and Health from Better Indoor Environments. *Indoor Air*. 1997;7:158-172.

Abstract: The existing literature contains strong evidence that characteristics of buildings and indoor environments significantly influence rates of respiratory disease, allergy and asthma symptoms, sick building symptoms, and worker performance. Theoretical considerations, and

limited empirical data, suggest that existing technologies and procedures can improve indoor environments in a manner that significantly increases health and productivity. At present, we can develop only crude estimates of the magnitude of productivity gains that may be obtained by providing better indoor environments; however, the projected gains are very large. For the U.S., we estimate potential annual savings and productivity gains of \$6 billion to \$19 billion from reduced respiratory disease; \$1 billion to \$4 billion from reduced allergies and asthma, \$10 billion to \$20 billion from reduced sick building syndrome symptoms, and \$12 billion to \$125 billion from direct improvements in worker performance that are unrelated to health. Sample calculations indicate that the potential financial benefits of improving indoor environments exceed costs by a factor of 18 to 47. The policy implications of the findings are discussed and include a recommendation for additional research

- (81) Hodgson M, Brodt W, Henderson D et al. Needs and opportunities for improving the health, safety, and productivity of medical research facilities. *Environ Health Perspect.* 2000;108 Suppl 6:1003-8.:1003-1008.

Abstract: Medical research facilities, indeed all the nation's constructed facilities, must be designed, operated, and maintained in a manner that supports the health, safety, and productivity of the occupants. The National Construction Goals, established by the National Science and Technology Council, envision substantial improvements in occupant health and worker productivity. The existing research and best practices case studies support this conclusion, but too frequently building industry professionals lack the knowledge to design, construct, operate, and maintain facilities at these optimum levels. There is a need for more research and more collaborative efforts between medical and facilities engineering researchers and practitioners in order to attain the National Construction Goals. Such collaborative efforts will simultaneously support attainment of the National Health Goals. This article is the summary report of the Healthy Buildings Committee for the Leadership Conference: Biomedical Facilities and the Environment sponsored by the National Institutes of Health, the National Association of Physicians for the Environment, and the Association of Higher Education Facilities Officers on 1--2 November 1999 in Bethesda, Maryland, USA

- (82) Hedge A, Mitchell GE, McCarthy JF, Ludwig J. Effects of a Furniture-integrated Breathing-zone Filtration System on Indoor Air Quality, Sick Building Syndrome, and Productivity. *Indoor Air.* 1993;3:328-336.

Abstract: Abstract A field experiment evaluated the effect of a furniture-integrated breathing-zone filtration (BZF) system on indoor air quality, worker comfort, health, and productivity. The BZF system tested filters office air to remove volatile organic compounds and airborne particulates. The BZF system was installed on one floor of a 29 story air-conditioned office building. Another floor of the building served as a control. Comparisons of pre-installation and three month post-installation surveys showed improvements in indoor air quality, sick building syndrome symptoms, and self-reported productivity with the BZF system References

- (83) Wargocki P, Sundell J, Bischof W et al. Ventilation and health in non-industrial indoor environments: report from a European Multidisciplinary Scientific Consensus Meeting (EUROVEN). *Indoor Air.* 2002;12:113-128.

Abstract: Abstract Scientific literature on the effects of ventilation on health, comfort, and productivity in non-industrial indoor environments (offices, schools, homes, etc.) has been reviewed by a multidisciplinary group of European scientists, called EUROVEN, with expertise in medicine, epidemiology, toxicology, and engineering. The group reviewed 105 papers published in peer-reviewed scientific journals and judged 30 as conclusive, providing sufficient

information on ventilation, health effects, data processing, and reporting, 14 as providing relevant background information on the issue, 43 as relevant but non-informative or inconclusive, and 18 as irrelevant for the issue discussed. Based on the data in papers judged conclusive, the group agreed that ventilation is strongly associated with comfort (perceived air quality) and health [Sick Building Syndrome (SBS) symptoms, inflammation, infections, asthma, allergy, short-term sick leave], and that an association between ventilation and productivity (performance of office work) is indicated. The group also concluded that increasing outdoor air supply rates in non-industrial environments improves perceived air quality; that outdoor air supply rates below 25 l/s per person increase the risk of SBS symptoms, increase short-term sick leave, and decrease productivity among occupants of office buildings; and that ventilation rates above 0.5 air changes per hour (h⁻¹) in homes reduce infestation of house dust mites in Nordic countries. The group concluded additionally that the literature indicates that in buildings with air-conditioning systems there may be an increased risk of SBS symptoms compared with naturally or mechanically ventilated buildings, and that improper maintenance, design, and functioning of air-conditioning systems contributes to increased prevalence of SBS symptoms. Practical Implications Ventilation requirements in many existing guidelines and standards may be too low to protect occupants of offices, schools, and homes from health and comfort problems and may not be optimal for human productivity. Higher ventilation rates can increase energy costs in relation to building operation, but these can be reduced by lowering pollution loads on the air indoors, e.g., by prudent and systematic maintenance of heating/ventilation/air-conditioning (HVAC) systems and by reducing superfluous pollution sources indoors. Energy costs can also be reduced by using efficient heat recovery systems. Source control and new ways of conditioning air are required

- (84) Bako-Biro Z, Wargocki P, Weschler CJ, Fanger PO. Effects of pollution from personal computers on perceived air quality, SBS symptoms and productivity in offices. *Indoor Air*. 2004;14:178-187.

Abstract: In groups of six, 30 female subjects were exposed for 4.8 h in a low-polluting office to each of two conditions--the presence or absence of 3-month-old personal computers (PCs). These PCs were placed behind a screen so that they were not visible to the subjects. Throughout the exposure the outdoor air supply was maintained at 10 l/s per person. Under each of the two conditions the subjects performed simulated office work using old low-polluting PCs. They also evaluated the air quality and reported Sick Building Syndrome (SBS) symptoms. The PCs were found to be strong indoor pollution sources, even after they had been in service for 3 months. The sensory pollution load of each PC was 3.4 olf, more than three times the pollution of a standard person. The presence of PCs increased the percentage of people dissatisfied with the perceived air quality from 13 to 41% and increased by 9% the time required for text processing. Chemical analyses were performed to determine the pollutants emitted by the PCs. The most significant chemicals detected included phenol, toluene, 2-ethylhexanol, formaldehyde, and styrene. The identified compounds were, however, insufficient in concentration and kind to explain the observed adverse effects. This suggests that chemicals other than those detected, so-called 'stealth chemicals', may contribute to the negative effects. PRACTICAL IMPLICATIONS: PCs are an important, but hitherto overlooked, source of pollution indoors. They can decrease the perceived air quality, increase SBS symptoms and decrease office productivity. The ventilation rate in an office with a 3-month-old PC would need to be increased several times to achieve the same perceived air quality as in a low-polluting office with the PC absent. Pollution from PCs has an important negative impact on the air quality, not only in offices but also in many other spaces, including homes. PCs may have played a role in previously published studies on SBS and perceived air quality, where PCs were overlooked as a

possible pollution source in the indoor environment. The fact that the chemicals identified in the office air and in the chamber experiments were insufficient to explain the adverse effects observed during human exposures illustrates the inadequacy of the analytical chemical methods commonly used in indoor air quality investigations. For certain chemicals the human senses are much more sensitive than the chemical methods routinely used in indoor air quality investigations. The adverse effects of PC-generated air pollutants could be reduced by modifications in the manufacturing process, increased ventilation, localized PC exhaust, or personalized ventilation systems

- (85) Daisey JM, Angell WJ, Apte MG. Indoor air quality, ventilation and health symptoms in schools: an analysis of existing information. *Indoor Air*. 2003;13:53-64.
Abstract: Abstract We reviewed the literature on Indoor Air Quality (IAQ), ventilation, and building-related health problems in schools and identified commonly reported building-related health symptoms involving schools until 1999. We collected existing data on ventilation rates, carbon dioxide (CO₂) concentrations and symptom-relevant indoor air contaminants, and evaluated information on causal relationships between pollutant exposures and health symptoms. Reported ventilation and CO₂ data strongly indicate that ventilation is inadequate in many classrooms, possibly leading to health symptoms. Adequate ventilation should be a major focus of design or remediation efforts. Total volatile organic compounds, formaldehyde (HCHO) and microbiological contaminants are reported. Low HCHO concentrations were unlikely to cause acute irritant symptoms (<0.05 ppm), but possibly increased risks for allergen sensitivities, chronic irritation, and cancer. Reported microbiological contaminants included allergens in deposited dust, fungi, and bacteria. Levels of specific allergens were sufficient to cause symptoms in allergic occupants. Measurements of airborne bacteria and airborne and surface fungal spores were reported in schoolrooms. Asthma and 'sick building syndrome' symptoms are commonly reported. The few studies investigating causal relationships between health symptoms and exposures to specific pollutants suggest that such symptoms in schools are related to exposures to volatile organic compounds (VOCs), molds and microbial VOCs, and allergens. Practical Implications The paper summarizes and explores the peer-reviewed literature on Indoor Air Quality (IAQ) in schools, a field that is of increasing interest to the research community, educators and school facilities managers, and the public at large. These experts generally agree that healthy indoor school environments are a necessity if a high standard of education is to be expected. Although peer-reviewed literature on this subject is sparse, there is a clear indication that classroom ventilation is typically inadequate. Researchers observed specific allergens in classrooms at levels sufficient to affect sensitive occupants. Studies of health symptom associations with IAQ conditions in the classroom are very rare, but taken with more general knowledge of IAQ, suggest that improved ventilation and targeted indoor pollutant source reductions could reduce certain occupant symptoms and improve the standard of health of the occupants
- (86) Mendell MJ, Heath GA. Do indoor pollutants and thermal conditions in schools influence student performance? A critical review of the literature. *Indoor Air*. 2005;15:27-52.
Abstract: Abstract To assess whether school environments can adversely affect academic performance, we review scientific evidence relating indoor pollutants and thermal conditions, in schools or other indoor environments, to human performance or attendance. We critically review evidence for direct associations between these aspects of indoor environmental quality (IEQ) and performance or attendance. Secondarily, we summarize, without critique, evidence on indirect connections potentially linking IEQ to performance or attendance. Regarding direct associations, little strongly designed research was available. Persuasive evidence links higher

indoor concentrations of NO₂ to reduced school attendance, and suggestive evidence links low ventilation rates to reduced performance. Regarding indirect associations, many studies link indoor dampness and microbiologic pollutants (primarily in homes) to asthma exacerbations and respiratory infections, which in turn have been related to reduced performance and attendance. Also, much evidence links poor IEQ (e.g. low ventilation rate, excess moisture, or formaldehyde) with adverse health effects in children and adults and documents dampness problems and inadequate ventilation as common in schools. Overall, evidence suggests that poor IEQ in schools is common and adversely influences the performance and attendance of students, primarily through health effects from indoor pollutants. Evidence is available to justify (i) immediate actions to assess and improve IEQ in schools and (ii) focused research to guide IEQ improvements in schools. Practical Implications There is more justification now for improving IEQ in schools to reduce health risks to students than to reduce performance or attendance risks. However, as IEQ-performance links are likely to operate largely through effects of IEQ on health, IEQ improvements that benefit the health of students are likely to have performance and attendance benefits as well. Immediate actions are warranted in schools to prevent dampness problems, inadequate ventilation, and excess indoor exposures to substances such as NO₂ and formaldehyde. Also, siting of new schools in areas with lower outdoor pollutant levels is preferable

- (87) Health Canada. Indoor Air Quality - Tools for Schools Action Kit for Canadian Schools. 2003. http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/air/tools_school-ouils_ecoles/tools_school-ouils_ecoles_e.pdf
- (88) Smith RC. The Biopsychosocial Revolution Interviewing and Provider-patient Relationships Becoming Key Issues for Primary Care. *J Gen Intern Med* 17[4], 309-310. 2002. <http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1495036&blobtype=pdf> available from <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1495036>
Abstract: George Engel proposed the biopsychosocial model in what soon became a landmark event for understanding medicine as a science. The model prompted a revolution in medical thinking by providing an argument and rationale that better linked medicine to science. Following the revolution in physics at the turn of the last century, science gradually moved away from previous linear, cause-effect thinking. To that point, understandably, medicine's guiding biomedical model focused only on diseases. Beginning with Engel's model, medical thinking has slowly evolved by incorporating and integrating psychosocial components. The biopsychosocial model stems from what many consider the modern articulation of science, general system theory. Engel's model prescribes a fundamentally different path from the still-guiding biomedical model: to be scientific, a model for medicine must include the psychosocial dimensions (personal, emotional, family, community) in addition to the biological aspects (diseases) of all patients.
- (89) Meggs WJ, Elsheik T, Metzger WJ, Albernaz M, Bloch RM. Nasal pathology and ultrastructure in patients with chronic airway inflammation (RADS and RUDS) following an irritant exposure. *J Toxicol Clin Toxicol.* 1996;34:383-396.
Abstract: BACKGROUND: Reactive airways dysfunction syndrome is a chronic asthma-like condition developing after an acute irritant exposure, and chronic inflammation has been seen on endobronchial biopsy. Reactive upper-airways dysfunction syndrome is chronic rhinitis developing in temporal association with a toxic inhalation exposure, but the pathophysiology is unknown. OBJECTIVES: To study biopsies of the nasal mucosa in patients with reactive upper-airways dysfunction syndrome and in some cases reactive airways dysfunction syndrome

developing in temporal association with a chlorine dioxide exposure, to see if a histologic basis for the persistent rhinitis and sensitivity to chemical irritants could be determined. **METHODS:** Specimens were stained with hematoxylin-eosin and immunoperoxidase stains for substance P, vasointestinal peptide, and S-100 (nerve fibers), and fixed in glutaraldehyde for electron microscopy. Biopsies of three nonexposed subjects were performed for comparison. A pathologist blinded to clinical data interpreted the specimens. **RESULTS:** Inflammation ratings of exposed individuals were higher than for the nonexposed individuals. The number of nerve fibers stained was greater for patients vs controls. Substance P and vasointestinal peptide staining was nonspecific. Electron microscopy showed desquamation of the epithelium and permeability of epithelial cell junctions. **CONCLUSION:** This study suggests a mechanism by which ongoing low level exposures perpetuate airway inflammation after an inducing toxic inhalation. A possible overlap between reactive airways dysfunction syndrome, reactive upper-airway dysfunction syndrome and the multiple chemical sensitivity syndrome is suggested

- (90) Millqvist E, Ternesten-Hasseus E, Stahl A, Bende M. Changes in levels of nerve growth factor in nasal secretions after capsaicin inhalation in patients with airway symptoms from scents and chemicals. *Environ Health Perspect.* 2005;113:849-852.
Abstract: Patients complaining of upper and lower airway symptoms caused by scents and chemicals have previously been shown to have increased cough sensitivity to inhaled capsaicin, but the precise mechanisms behind this reaction are unknown. Hypothesizing that a neurochemical alteration related to sensory hyperreactivity (SHR) of the airway mucosa occurs, we measured levels of nerve growth factor (NGF) in nasal lavage fluid (NAL) before and after capsaicin inhalation provocations and related the capsaicin cough sensitivity to the NGF levels. Thirteen patients with SHR and 14 control subjects were provoked with capsaicin inhalation at three different doses. We measured NGF in NAL before and after provocation and recorded cough and capsaicin-induced symptoms. All subjects demonstrated a dose-dependent cough response to capsaicin inhalation, with a more pronounced effect in patients than in controls. Basal levels of NGF were significantly lower in the patient group than in the control subjects ($p < 0.01$). After capsaicin provocation, the patients showed a significant increase in NGF ($p < 0.01$), which was related to capsaicin cough sensitivity. The findings demonstrate that, in patients with airway symptoms induced by scents and chemicals, SHR is real and measurable, demonstrating a pathophysiology in the airways of these patients compared to healthy subjects
- (91) Kimata H. Effect of exposure to volatile organic compounds on plasma levels of neuropeptides, nerve growth factor and histamine in patients with self-reported multiple chemical sensitivity. *Int J Hyg Environ Health.* 2004;207:159-163.
Abstract: Plasma levels of substance P, vasoactive intestinal peptide and nerve growth factor, but not histamine, were elevated in patients with self-reported multiple chemical sensitivity (sMCS). Exposure to volatile organic compounds (VOC) increased plasma levels of all parameters in these patients, while it had no effect in normal subjects or patients with atopic eczema/dermatitis syndrome (AEDS). Exposure to VOC also enhanced skin wheal responses induced by histamine in patients with sMCS, while it failed to do so in normal or AEDS subjects. These results indicate that exposure to VOC may enhance neurogenic inflammation with concomitant enhancement of histamine-induced responses
- (92) Interian A, Gara MA, az-Martinez AM et al. The value of pseudoneurological symptoms for assessing psychopathology in primary care. *Psychosom Med.* 2004;66:141-146.
Abstract: **OBJECTIVE:** This study sought to examine the relationship between pseudoneurological symptoms (PNS) and somatic and psychiatric symptom severity, physical

functioning, and psychiatric comorbidity. **METHODS:** Interview and questionnaire data were obtained from 120 patients with somatization who participated in a study assessing the efficacy of cognitive-behavioral therapy. Measures elicited information on psychiatric diagnoses, anxiety and depressive symptom levels, somatic symptoms, and physical functioning. Statistical analyses examined the relationship between PNS and the diagnosis of somatization disorder, physical and psychiatric symptom severity, and psychiatric comorbidity. **RESULTS:** Roughly half of the sample had a history of four or more PNS. Results showed that having four or more PNS was not predictive of somatization disorder. However, having four or more PNS was found to be significantly correlated with the severity of anxiety, depression, somatic complaints, and physical dysfunction. These associations were identified while controlling for the symptom count of nonpseudoneurological symptoms, the presence of somatization disorder, and the presence of chronic painful physical conditions. In addition, having four or more PNS was significantly associated with a higher likelihood of receiving a diagnosis of major depression, dysthymia, panic disorder, and generalized anxiety disorder. **CONCLUSIONS:** A history of four or more PNS is common among somatizing patients in primary care and associated with a more severe clinical presentation, even after controlling for other factors known to be associated with severity. Four or more PNS may identify a distinct subgroup of somatization and serve as a clinical indicator for identifying psychiatric disorders in primary care. Future studies should explore the assessment of PNS using briefer measures. Furthermore, PNS should be evaluated with samples more representative of US primary care populations, as well as samples that include adequate representation from other ethnic backgrounds (eg, African-American, Asian, etc.)

- (93) Ford CV. Somatization and fashionable diagnoses: illness as a way of life. *Scand J Work Environ Health*. 1997;23 Suppl 3:7-16.:7-16.

Abstract: The history of "nondisease" dates back, at least 4000 years, to early descriptions of hysteria. More recently somatization became a part of the official diagnostic nomenclature by creation of the DSM III category, "somatoform disorders." Somatization can serve as a rationalization for psychosocial problems or as a coping mechanism, and for some illness, becomes a way of life. One variation of somatization can be the "fashionable diagnosis", for example, fibromyalgia, multiple chemical sensitivities, dysautonomia, and, in the past, "reactive hypoglycemia". These disorders are phenomenologically related to environmental or occupational syndromes and mass psychogenic illness. Fashionable illnesses are characterized by (i) vague, subjective multisystem complaints, (ii) a lack of objective laboratory findings, (iii) quasi-scientific explanations, (iv) overlap from one fashionable diagnosis to another, (v) symptoms consistent with depression or anxiety or both, (vi) denial of psychosocial distress or attribution of it to the illness. Fashionable diagnoses represent a heterogeneous collection of physical diseases, somatization, and anxiety or depression. They are final common symptomatic pathways for a variety of influences including environmental factors, intrapersonal distress and solutions to social problems. A fashionable diagnosis allows psychosocial distress to be comfortably hidden from both the patient and the physician, but premature labeling can also mask significant physical disease. Hysteria remains alive and well and one contemporary hiding place is fashionable illness

- (94) Chang C, Gershwin ME. Indoor air quality and human health: truth vs mass hysteria. *Clin Rev Allergy Immunol*. 2004;27:219-239.

Abstract: Indoor air quality is an important issue, because anything we breathe can potentially affect our health. To determine if there is a real health risk, well-designed scientifically valid studies must be performed. Although much attention has focused on sick building syndrome,

chemical sensitivities, and mycotoxicosis, there actually is very little evidence that these conditions have an adverse effect on human health. In contrast, real health issues have been shown to exist regarding indoor air triggers of allergies and asthma. Outdoor allergens are difficult to avoid because the pollen grains we encounter outdoors, which are the size that can cause allergies, are windborne and can travel for miles. However, indoor allergens can cause severe allergic symptoms and may also have a priming effect on an individual's susceptibility to simultaneous or subsequent exposure of other outdoor allergens. Therefore, it is important to minimize exposure to indoor allergens. Determination of individual susceptibility can be paired with knowledge of the patient's indoor exposure pattern to produce a customized management plan of avoidance, which can be used in conjunction with pharmacological treatment of allergies and asthma, as well as immunotherapy

- (95) Staudenmayer H, Binkley KE, Leznoff A, Phillips S. Idiopathic environmental intolerance: Part 1: A causation analysis applying Bradford Hill's criteria to the toxicogenic theory. *Toxicol Rev.* 2003;22:235-246.

Abstract: Idiopathic environmental intolerance (IEI) is a descriptor for a phenomenon that has many names including environmental illness, multiple chemical sensitivity and chemical intolerance. Toxicogenic and psychogenic theories have been proposed to explain IEI. This paper presents a causality analysis of the toxicogenic theory using Bradford Hill's nine criteria (strength, consistency, specificity, temporality, biological gradient, biological plausibility, coherence, experimental intervention and analogy) and an additional criteria (reversibility) and reviews critically the scientific literature on the topic. The results of this analysis indicate that the toxicogenic theory fails all of these criteria. There is no convincing evidence to support the fundamental postulate that IEI has a toxic aetiology; the hypothesised biological processes and mechanisms are implausible

- (96) Staudenmayer H, Binkley KE, Leznoff A, Phillips S. Idiopathic environmental intolerance: Part 2: A causation analysis applying Bradford Hill's criteria to the psychogenic theory. *Toxicol Rev.* 2003;22:247-261.

Abstract: Toxicogenic and psychogenic theories have been proposed to explain idiopathic environmental intolerance (IEI). Part 2 of this article is an evidence-based causality analysis of the psychogenic theory using an extended version of Bradford Hill's criteria. The psychogenic theory meets all of the criteria directly or indirectly and is characterised by a progressive research programme including double-blind, placebo-controlled provocation challenge studies. We conclude that IEI is a belief characterised by an overvalued idea of toxic attribution of symptoms and disability, fulfilling criteria for a somatoform disorder and a functional somatic syndrome. A neurobiological diathesis similar to anxiety, specifically panic disorder, is a neurobiologically plausible mechanism to explain triggered reactions to ambient doses of environmental agents, real or perceived. In addition, there is a cognitively mediated fear response mechanism characterised by vigilance for perceived exposures and bodily sensations that are subsequently amplified in the process of learned sensitivity. Implications for the assessment and treatment of patients are presented

- (97) Davidoff AL, Fogarty L. Psychogenic origins of multiple chemical sensitivities syndrome: a critical review of the research literature. *Arch Environ Health.* 1994;49:316-325.

Abstract: The purpose of this review was to critically evaluate research on the psychogenic origins of multiple chemical sensitivities (MCS) syndrome. Using as keywords environmental illness, multiple chemical sensitivities, and clinical ecology, two databases--PsychLit and Medline--were searched by computer; reference lists of all articles located were also searched

manually. Ten articles meeting three criteria were selected for review. Five sample selection problems, seven measurement problems, and three study design problems were common in all but one of the articles reviewed. Current studies investigating psychogenic hypotheses of MCS syndrome are methodologically problematic and their conclusions questionable. Studies of psychiatric profiles observed in MCS syndrome need to be designed to differentiate between competing psychogenic and biogenic hypotheses

- (98) Leznoff A. Provocative challenges in patients with multiple chemical sensitivity. *J Allergy Clin Immunol.* 1997;99:438-442.
Abstract: Whether multiple chemical sensitivity (MCS) is an organic disease initiated by environmental exposure or a psychologic disorder is a subject of controversy. The identification of pathophysiologic or psychophysiologic mechanisms occurring in patients with MCS after provocative challenges should be illuminating. Fifteen patients with MCS were challenged with their trigger substances and observed clinically. Prechallenge and postchallenge pulmonary function tests and PCO₂, PO₂, and oxygen saturation were measured. All of the patients whose symptoms were reproduced by the challenge (11 of 15) showed clinical evidence of acute hyperventilation with a rapid fall in PCO₂ and no change or a rise in oxygen saturation. The symptoms and signs were consistent with an anxiety reaction with hyperventilation. Pulmonary function was unchanged; and recovery was rapid, aided in two cases by rebreathing into a paper bag. The most logical conclusion is that in these patients the MCS disorder is a manifestation of an anxiety syndrome triggered by their perception of an environmental insult, with at least some of their symptoms induced by hyperventilation
- (99) Leznoff A, Binkley KE. Idiopathic environmental intolerances: results of challenge studies. *Occup Med.* 2000;15:529-537.
Abstract: It has been postulated that psychophysiologic mechanisms may account for symptom generation in IEI. In this review, the similarity of IEI and panic disorder symptoms are noted. The results of various challenge studies, both with known panicogenic substances and self-identified triggers, are examined. Available data are consistent with the premise that IEI symptoms have a psychophysiologic basis
- (100) Fiedler N, Kipen HM, DeLuca J, Kelly-McNeil K, Natelson B. A controlled comparison of multiple chemical sensitivities and chronic fatigue syndrome. *Psychosom Med.* 1996;58:38-49.
Abstract: The present study had two objectives: 1) to determine the characteristics that differentiated subjects with multiple chemical sensitivities (MCS), chemical sensitivities (CS), and chronic fatigue syndrome (CFS); and 2) to evaluate the psychiatric and neuropsychological complaints of these groups relative to normal controls. A cross-sectional comparison was made of the following groups matched for age, sex, and education: 1) patients whose sensitivities to multiple low level chemical exposures began with a defined exposure (MCS; N = 23); 2) patients with sensitivities to multiple chemicals without a clear date of onset (CS; N = 13); 3) patients meeting CDC criteria for Chronic Fatigue Syndrome (CFS; N = 18); and 4) normal controls (N = 18). Subjects with sensitivities to chemicals (MCS and CS) reported significantly more lifestyle changes due to chemical sensitivities and significantly more chemical substances that made them ill compared with chronic fatigue and normal controls. MCS, CS, and CFS patients had significantly higher rates of current psychiatric disorders than normal controls and reported significantly more physical symptoms with no medical explanation. Seventy-four percent of MCS and 61% of CFS did not qualify for any current Axis I psychiatric diagnosis. Chemically sensitive subjects without a defined date of onset (CS) had the highest rate of Axis I psychiatric disorders (69%). On the MMPI-2, 44% of MCS, 42% of CS, 53% of CFS, and none

of the controls achieved clinically significant elevations on scales associated with somatoform disorders. With the exception of one complex test of visual memory, no significant differences were noted among the groups on tests of neuropsychological function. Standardized measures of psychiatric and neuropsychological function did not differentiate subjects with sensitivities to chemicals from those with chronic fatigue. Subjects with sensitivities to chemicals and no clear date of onset had the highest rate of psychiatric morbidity. Standardized neuropsychological tests did not substantiate the cognitive impairment reported symptomatically. Cognitive deficits may become apparent under controlled exposure conditions

- (101) Fiedler N. Neuropsychological approaches for the detection and evaluation of toxic symptoms. *Environ Health Perspect.* 1996;104 Suppl 2:239-45.:239-245.
Abstract: The purpose of this paper is 3-fold: a) to review briefly the neuropsychological tests that have been used to evaluate the effects of neurotoxicants; b) to identify individual factors that may create heightened sensitivity to neurotoxicants; and c) to discuss test parameters that will increase the sensitivity of neuropsychological tests for detecting symptoms in low-level exposure situations. While the body of literature on neurobehavioral toxicology has increased dramatically during the past 10 years, it remains difficult to discern which tests are most effective in detecting behavioral effects even among workers with significant exposures. Few investigators have evaluated the interactions between individual differences, such as gender and psychiatric function, and exposure to neurotoxicants. Detection of behavioral performance decrements among uniquely susceptible populations such as those with sensitivities to low-level exposures (e.g., multiple chemical sensitivities) will require more difficult tests than are frequently used in current neuropsychological test batteries
- (102) Fiedler N, Maccia C, Kipen H. Evaluation of chemically sensitive patients. *J Occup Med.* 1992;34:529-538.
Abstract: An increasing number of patients have been presenting with multiple symptoms they attribute to low-level chemical exposures, ie, multiple chemical sensitivities (MCS). Although some studies have evaluated such patients, the selection criteria has not been rigorously defined. The present study is the first to use a relatively rigorous definition of MCS to select patients for study. Comprehensive evaluation of medical, psychiatric, neuropsychological, and immunological status of a series of MCS patients is presented. In contrast to previous studies, patients in this study did not have a history of psychiatric disorder. However, some patients were currently depressed. Neuropsychological assessment did not reveal any abnormalities with the exception of one test of verbal memory for which performance was consistently poor relative to the normative sample. No significant immunological abnormalities were noted
- (103) Bornschein S, Hausteiner C, Konrad F, Forstl H, Zilker T. Psychiatric morbidity and toxic burden in patients with environmental illness: a controlled study. *Psychosom Med.* 2006;68:104-109.
Abstract: OBJECTIVE: Patients with environmental illness experience a large number of psychological symptoms. The nature of these symptoms and their pathogenesis (toxicogenic versus psychogenic) is controversial. The objective was to (1) characterize the nature of the psychological symptoms according to well-established diagnostic criteria, and (2) to investigate the association between toxicological factors and psychological symptoms. METHODS: Toxic burden, somatic morbidity, and psychiatric morbidity were assessed in 309 outpatients with environmental illness and 59 semiconductor industry workers matched for age and gender. Psychiatric disorders were assessed by a structured psychiatric interview (SCID), and distress was assessed by the Symptom-Checklist-90-Revised (SCL-90-R). Routine and specific

laboratory tests in blood and urine samples were used to assess chemical exposures. RESULTS: Overall psychiatric morbidity was significantly higher in patients than in controls according to SCID (75% versus 24%). Somatoform, mood, and anxiety disorders were significantly more frequent in patients with environmental illness. They also revealed marked stress on the SCL-90-R somatization subscale and scored significantly higher than controls on most of the other subscales. Industry workers from the control group tended to have higher urine metal concentrations than environmental illness patients and similar concentrations of solvents in blood. CONCLUSION: Our data extend previous findings of high psychiatric morbidity in patients with environmental illness. They do not support the notion of a direct causal link between chemical exposure and the psychological symptoms

- (104) Department of Health and Human Services Centers for Disease Control and Prevention. Third National Report on Human Exposure to Environmental Chemicals. USA Centers for Disease Control and Prevention . 2005. www.cdc.gov/exposurereport/3rd/pdf/thirdreport.pdf
Abstract: The Third Report presents new data on the exposure of the U.S. population to environmental chemicals. The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical causes disease. Advances in analytical methods allow us to measure lower and lower levels of environmental chemicals in people. Separate studies of varying exposure levels and health effects are required to determine which blood and urine levels are safe and which result in disease.
Chemicals in the Report were selected on the basis of scientific data that suggested exposure in the U.S. population; the seriousness of health effects known or suspected to result from some levels of exposure; the need to assess the efficacy of public health actions to reduce exposure to a chemical; the availability of a biomonitoring analytical method with adequate accuracy, precision, sensitivity, specificity, and throughput; the availability of adequate blood or urine samples; and the incremental analytical cost to perform the biomonitoring analysis for the chemical. The availability of biomonitoring methods with adequate performance and acceptable cost was a major consideration.
We have not performed statistical tests for trends over time given that data are available only for the 1999-2000 and 2001-2002 survey periods. New data will be released for the U.S. population every 2 years, with the next release covering the survey period 2003-2004. With additional data points it will be possible to describe patterns over time and in some cases test for trends. We plan to investigate trends in future Reports for chemicals that have at least 3 survey periods.
- (105) Baldwin DR and Marshall WJ. Heavy metal poisoning and its laboratory investigation. *Ann Clin Biochem* 36, 267-300. 1999.
Abstract: The term 'heavy metal' is, in this context, imprecise. It should probably be reserved for those elements with an atomic mass of 200 or greater [e.g., mercury (200), thallium (204), lead (207), bismuth (209) and the thorium series]. In practice, the term has come to embrace any metal, exposure to which is clinically undesirable and which constitutes a potential hazard. Our intention in this review is to provide an overview of some general concepts of metal toxicology and to discuss in detail metals of particular importance, namely, cadmium, lead, mercury, thallium, bismuth, arsenic, antimony and tin. Poisoning from individual metals is rare in the UK, even when there is a known risk of exposure. Table 1 shows that during 1991±92 only 1.1% of male lead workers in the UK and 5.5% of female workers exceeded the legal limits for blood lead concentration. Collectively, however, poisoning with metals forms an important aspect of toxicology because of their widespread use and availability. Furthermore, hitherto unrecognized hazards and accidents continue to be described. The investigation of

metal poisoning forms a distinct specialist area, since most metals are usually measured using atomic absorption techniques. Analyses require considerable expertise and meticulous attention to detail to ensure valid results. Different analytical performance standards may be required of assays used for environmental and occupational monitoring, or for solely toxicological purposes. Because of the high capital cost of good quality instruments, the relatively small numbers of tests required and the variety of metals, it is more cost-effective if such testing is carried out in regional, national or other centres having the necessary experience. Nevertheless, patients are frequently cared for locally, and clinical bio-chemists play a crucial role in maintaining a high index of suspicion and liaising with clinical colleagues to ensure the provision of correct samples for analysis and timely advice.

- (106) Araki S, Sakai T, Sato H, Kaneko T, Sakai R, Yokoyama K. [Multiple chemical sensitivities: case definition, etiology and relations to allergy, poisoning, psychogenic illness etc]. *Nippon Koshu Eisei Zasshi*. 1999;46:769-778.
Abstract: Multiple Chemical Sensitivities (MCS) have been defined as an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects; no single widely accepted test of physiologic function can be shown to correlate with symptoms (Cullen MR, 1987). The etiology of MCS is hypothesized as a toxicant-induced loss of tolerance to multiple chemicals with subsequent manifestation of multiple-organ symptoms triggered by low-level exposure to such chemicals. The involvement of multiple organs might be attributed to a neurogenic switching mechanism. The final diagnosis of MCS is to rely on provocation of symptoms in a exposure chamber by a double-blind method. Relations of MCS to allergy, poisoning, psychogenic illness, chemical sensitivity, idiopathic environmental intolerances etc. are discussed in terms of case definition and etiology of these disorders
- (107) Davidoff AL, Fogarty L, Keyl PM. Psychiatric inferences from data on psychologic/psychiatric symptoms in multiple chemical sensitivities syndrome. *Arch Environ Health*. 2000;55:165-175.
Abstract: When abnormal psychologic/psychiatric symptom data are obtained on personality tests or psychiatric interviews administered to patients who report symptoms of Multiple Chemical Sensitivities Syndrome, investigators typically attribute these to either psychiatric traits or to psychogenic origins of illness. The primary purpose of these studies was the evaluation of the plausibility of nonpsychiatric explanations of psychologic/psychiatric symptom data. In Study 1, patients with Multiple Chemical Sensitivities Syndrome used the Minnesota Multiphasic Personality Inventory 2 (MMPI-2) to describe which items had changed after they developed the condition. In Study 2, three diverse groups of professionals predicted which items on the MMPI-2 might change after a mentally healthy person developed the Syndrome or a condition resembling it. In Study 3, a second sample of Multiple Chemical Sensitivities Syndrome patients completed the MMPI-2 and other questionnaires by mail, which allowed the authors to ascertain whether these patients showed more or different psychopathology than was described by patients and hypothesized by professionals. Data from Study 1 patient informants indicated that developing the syndrome might result in a psychopathological MMPI-2 profile, characterized by abnormal Hypochondriasis and Hysteria scale scores. Professionals in Study 2 showed a consensus about hypothesized MMPI-2 changes following the development of the syndrome. These changes likely elevated the Hypochondriasis, Hysteria, Psychasthenia, Depression, and Schizophrenia scale scores. In Study 3, the patients taking the MMPI-2 showed elevations on the Hypochondriasis, Hysteria, Depression (women only), and Schizophrenia scales. Abnormal scores were associated closely

with greater severity of illness and greater adjustment to illness. The strategy of administering psychometric tests to ill populations for the purposes of evaluating psychiatric illness or traits, and/or psychogenic origins of illness was shown to be potentially misleading

- (108) Poonai NP, Antony MM, Binkley KE et al. Psychological features of subjects with idiopathic environmental intolerance. *J Psychosom Res.* 2001;51:537-541.
Abstract: OBJECTIVES: Idiopathic environmental intolerance (IEI) is associated with unexplained symptoms attributed to non-noxious levels of environmental substances. Clinically, some of the symptoms of IEI overlap with those of panic disorder (PD). We have recently reported a link between IEI and panic responses to a single inhalation of 35% carbon dioxide (CO₂), a reliable panic induction challenge. This study assessed depression, stress, anxiety, and agoraphobic symptoms among IEI subjects from our previous study versus healthy controls. METHODS: Thirty-six IEI and 37 control subjects with no preexisting psychiatric history were compared on self-report psychological questionnaires. RESULTS: IEI subjects scored significantly higher than controls on the Agoraphobic Cognitions Questionnaire (ACQ), Depression Anxiety Stress Scales (DASS), and Mobility Inventory for Agoraphobia (MI) (Student's t, P<.05). CONCLUSIONS: IEI subjects represent a group with morbidity significantly higher than a control population but less than what would be expected for a clinical psychiatric population
- (109) Jason LA, Taylor RR, Kennedy CL. Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms. *Psychosom Med.* 2000;62:655-663.
Abstract: OBJECTIVE: The aim of this study was to determine illness comorbidity rates for individuals with chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivities (MCS). An additional objective was to identify characteristics related to the severity of fatigue, disability, and psychiatric comorbidity in each of these illness groups. METHODS: A random sample of 18,675 residents in Chicago, Illinois, was first interviewed by telephone. A control group and a group of individuals with chronic fatigue accompanied by at least four minor symptoms associated with CFS received medical and psychiatric examinations. RESULTS: Of the 32 individuals with CFS, 40.6% met criteria for MCS and 15.6% met criteria for FM. Individuals with MCS or more than one diagnosis reported more physical fatigue than those with no diagnosis. Individuals with more than one diagnosis also reported greater mental fatigue and were less likely to be working than those with no diagnosis. Individuals with CFS, MCS, FM, or more than one diagnosis reported greater disability than those with no diagnosis. CONCLUSIONS: Rates of coexisting disorders were lower than those reported in prior studies. Discrepancies may be in part attributable to differences in sampling procedures. People with CFS, MCS, or FM endure significant disability in terms of physical, occupational, and social functioning, and those with more than one of these diagnoses also report greater severity of physical and mental fatigue. The findings illustrate differences among the illness groups in the range of functional impairment experienced
- (110) Aaron LA, Buchwald D. Chronic diffuse musculoskeletal pain, fibromyalgia and co-morbid unexplained clinical conditions. *Best Pract Res Clin Rheumatol.* 2003;17:563-574.
Abstract: This chapter reviews our current knowledge on the presence of overlapping syndromes in one form of chronic diffuse pain, fibromyalgia. Patients with fibromyalgia often present with signs and symptoms of other unexplained clinical conditions, including chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, and multiple chemical sensitivities. The high prevalence, impact on function and opportunities for treatment

underscore the need for clinicians and researchers to screen routinely for co-morbid unexplained clinical conditions among persons with fibromyalgia. We, therefore, describe a simple approach to screening for such conditions in accordance with published criteria. Interventions should directly address both fibromyalgia symptoms and co-morbid unexplained clinical conditions, as well as the multiple factors that propagate pain, fatigue and limitations in function

- (111) Aaron LA, Herrell R, Ashton S et al. Comorbid clinical conditions in chronic fatigue: a co-twin control study. *J Gen Intern Med.* 2001;16:24-31.
Abstract: OBJECTIVES: Chronically fatiguing illness, defined as fatigue for at least 6 months, has been associated with various physical health conditions. Our objective was to determine whether there is a significant relationship between chronically fatiguing illness and 10 clinical conditions that frequently appear to be associated with fatigue, adjusting for the potentially confounding effects of psychiatric illness. DESIGN: A co-twin control study controlling for genetic and many environmental factors by comparing chronically fatigued twins with their nonfatigued co-twins. SETTING: A nationally distributed volunteer twin registry. PARTICIPANTS: The study included 127 twin pairs in which one member of the pair experienced fatigue of at least 6 months' duration and the co-twin was healthy and denied chronic fatigue. Fatigued twins were classified into 3 levels using increasingly stringent diagnostic criteria. MEASUREMENTS AND MAIN RESULTS: Twins reported on a history of fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities, temporomandibular disorder, interstitial cystitis, postconcussion syndrome, tension headache, chronic low back pain, chronic pelvic pain (women), and chronic nonbacterial prostatitis (men). The prevalence of these comorbid clinical conditions was significantly higher in the fatigued twins compared to their nonfatigued co-twins. Most notably, compared to their nonfatigued co-twins, the chronically fatigued twins had higher rates of fibromyalgia (> 70% vs < 10%) and irritable bowel syndrome (> 50% vs < 5%). The strongest associations were observed between chronic fatigue and fibromyalgia (odds ratios > 20), irritable bowel syndrome, chronic pelvic pain, multiple chemical sensitivities, and temporomandibular disorder (all with odds ratios > or = 4). Regression analysis suggested that the number of comorbid clinical conditions associated with chronic fatigue could not be attributed solely to psychiatric illness. CONCLUSIONS: Chronically fatiguing illnesses were associated with high rates of many other clinical conditions. Thus, patients with chronic fatigue may present a complex clinical picture that poses diagnostic and management challenges. Nonetheless, clinicians should assess such patients for the presence of comorbid clinical conditions. Future research should provide a better understanding of the temporal relationship of the onset of fatigue and these conditions, and develop strategies for early intervention
- (112) Black DW, Doebbeling BN, Voelker MD et al. Multiple chemical sensitivity syndrome: symptom prevalence and risk factors in a military population. *Arch Intern Med.* 2000;160:1169-1176.
Abstract: OBJECTIVE: To assess the prevalence of and risk factors for self-reported symptoms suggestive of multiple chemical sensitivities/idiopathic environmental intolerance (MCS/IEI) in Persian Gulf War (PGW) veterans from Iowa and a comparison group of PGW-era military personnel. METHODS: A population-based sample of Iowa military personnel was surveyed using a cross-sectional telephone interview. Study participants were randomly drawn from 1 of 4 domains: PGW active duty, PGW National Guard/Reserve, non-PGW active duty, and non-PGW National Guard/Reserve. A complex sample survey design was used selecting participants from the following substrata: age, sex, race, rank, and military branch. The criteria for MCS/IEI

were developed using expert consensus and the medical literature. RESULTS: A total of 3695 study participants (76% of those eligible) completed the telephone survey. The prevalence of symptoms suggestive of MCS/IEI in all participants was 3.4%. Veterans of the PGW reported a significantly higher prevalence of symptoms suggestive of MCS/IEI than did non-PGW military personnel (5.4% vs 2.6%); greater sensitivity to organic chemicals, vehicle exhaust, cosmetics, and smog; and more lifestyle changes. The following risk factors for MCS/IEI were identified with univariate analysis: deployment to the Persian Gulf, age (>25 years), female sex, receiving a physician diagnosis of MCS, previous professional psychiatric treatment, previous psychotropic medication use, current psychiatric illness, and a low level of preparedness. Multiple logistic regression analysis identified several independent risk factors for MCS/IEI, including deployment to the Persian Gulf, age, sex, rank, branch of service, previous professional psychiatric treatment, and current mental illness. CONCLUSIONS: Self-reported symptoms suggestive of MCS/IEI are relatively frequent in a military population and are more common among PGW veterans than comparable controls. Reported chemical sensitivities and accompanying behavioral changes were also frequent. After adjusting for age, sex, and training preparedness, previous professional psychiatric treatment and previous psychotropic medication use (before deployment) showed a robust association with symptoms suggestive of MCS

- (113) Beseler C, Stallones L. Safety practices, neurological symptoms, and pesticide poisoning. *J Occup Environ Med.* 2003;45:1079-1086.
Abstract: Depression, anxiety, inability to concentrate, and spatial disorientation associated with pesticide poisoning may influence farmers' ability to comply with established safety procedures. The purpose of this article is to describe the relationship between safety practices, neurological symptoms, and pesticide poisoning. A survey of farm residents was conducted in an eight-county area in Colorado. Multivariate logistic regression models were used to determine associations between safety practices, neurological symptoms, and previous pesticide poisoning. A number of safety practices were associated with the following neurological symptoms: difficulty concentrating; feeling irritable; relatives noticing memory difficulties; and difficulty understanding reading materials. The associations between safety practices and neurological symptoms were increased in the presence of pesticide poisoning. Factors associated with failure to engage in established safety practices in this study were neurological symptoms
- (114) Crago BR, Gray MR, Nelson LA, Davis M, Arnold L, Thrasher JD. Psychological, neuropsychological, and electrocortical effects of mixed mold exposure. *Arch Environ Health.* 2003;58:452-463.
Abstract: The authors assessed the psychological, neuropsychological, and electrocortical effects of human exposure to mixed colonies of toxigenic molds. Patients (N = 182) with confirmed mold-exposure history completed clinical interviews, a symptom checklist (SCL-90-R), limited neuropsychological testing, quantitative electroencephalogram (QEEG) with neurometric analysis, and measures of mold exposure. Patients reported high levels of physical, cognitive, and emotional symptoms. Ratings on the SCL-90-R were "moderate" to "severe," with a factor reflecting situational depression accounting for most of the variance. Most of the patients were found to suffer from acute stress, adjustment disorder, or post-traumatic stress. Differential diagnosis confirmed an etiology of a combination of external stressors, along with organic metabolically based dysregulation of emotions and decreased cognitive functioning as a result of toxic or metabolic encephalopathy. Measures of toxic mold exposure predicted QEEG measures and neuropsychological test performance. QEEG results included narrowed frequency bands and increased power in the alpha and theta bands in the frontal areas of the cortex. These

findings indicated a hypoactivation of the frontal cortex, possibly due to brainstem involvement and insufficient excitatory input from the reticular activating system. Neuropsychological testing revealed impairments similar to mild traumatic brain injury. In comparison with premorbid estimates of intelligence, findings of impaired functioning on multiple cognitive tasks predominated. A dose-response relationship between measures of mold exposure and abnormal neuropsychological test results and QEEG measures suggested that toxic mold causes significant problems in exposed individuals. Study limitations included lack of a comparison group, patient selection bias, and incomplete data sets that did not allow for comparisons among variables

- (115) Stallones L, Beseler C. Pesticide illness, farm practices, and neurological symptoms among farm residents in Colorado. *Environ Res.* 2002;90:89-97.
Abstract: The purpose of this study is to evaluate the association between pesticides and neurological symptoms among a population exposed to organophosphate chemicals as a result of agricultural use. Chronic sequelae of acute pesticide poisoning from organophosphate compounds include a variety of neurological symptoms including restlessness, irritability, and trouble sleeping. Individuals who have had an acute pesticide poisoning have been reported to suffer a wide range of neurological symptoms that occur from weeks to months after the initial episode. Data for this study came from a cross-sectional survey of farmers and their spouses conducted in an eight-county area in north-eastern Colorado. Neurological characteristics were assessed to determine their relationship with previously reported pesticide-related illnesses. Symptoms that were significantly associated with a previous poisoning were difficulty concentrating [OR 2.07, 95% confidence interval (CI) 1.22, 3.50]; relatives noticing person had trouble remembering things (OR 2.54, 95% CI 1.47, 4.39); making notes to remember things (OR 2.18, 95% CI 1.20, 3.97); finding it hard to understand the meaning of newspapers, magazines, and books (OR 1.90, 95% CI 1.01, 3.60); felt irritable (OR 1.84, 95% CI 1.08, 3.12); felt depressed (OR 2.82, 95% CI 1.65, 4.81); had heart palpitations without exertion (OR 2.83, 95% CI 1.22, 6.54); sleeping more than usual (OR 3.58, 95% CI 1.95, 6.58); difficulty moving fingers or grasping things (OR 2.08, 95% CI 1.06, 3.24); and headaches at least once a week (OR 1.85, 95% CI 1.06, 3.24). Stepwise regression was used to identify the best explanatory model of pesticide-related illness. Variables that were associated with increased odds of illness were being male, being depressed, sleeping too much, and using crop organophosphates
- (116) Anyanwu E, Campbell AW, Jones J, Ehiri JE, Akpan AI. The neurological significance of abnormal natural killer cell activity in chronic toxigenic mold exposures. *ScientificWorldJournal.* 2003;3:1128-37.:1128-1137.
Abstract: Toxigenic mold activities produce metabolites that are either broad-spectrum antibiotics or mycotoxins that are cytotoxic. Indoor environmental exposure to these toxigenic molds leads to adverse health conditions with the main outcome measure of frequent neuroimmunologic and behavioral consequences. One of the immune system disorders found in patients presenting with toxigenic mold exposure is an abnormal natural killer cell activity. This paper presents an overview of the neurological significance of abnormal natural killer cell (NKC) activity in chronic toxigenic mold exposure. A comprehensive review of the literature was carried out to evaluate and assess the conditions under which the immune system could be dysfunctionally interfered with leading to abnormal NKC activity and the involvement of mycotoxins in these processes. The functions, mechanism, the factors that influence NKC activities, and the roles of mycotoxins in NKCs were cited wherever necessary. The major presentations are headache, general debilitating pains, nose bleeding, fevers with body

temperatures up to 40 degrees C (104 degrees F), cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, vertigo/dizziness, and in some cases, seizures. Although sleep is commonly considered a restorative process that is important for the proper functioning of the immune system, it could be disturbed by mycotoxins. Most likely, mycotoxins exert some rigorous effects on the circadian rhythmic processes resulting in sleep deprivation to which an acute and transient increase in NKC activity is observed. Depression, psychological stress, tissue injuries, malignancies, carcinogenesis, chronic fatigue syndrome, and experimental allergic encephalomyelitis could be induced at very low physiological concentrations by mycotoxin-induced NKC activity. In the light of this review, it is concluded that chronic exposures to toxigenic mold could lead to abnormal NKC activity with a wide range of neurological consequences, some of which were headache, general debilitating pains, fever, cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, and seizures

- (117) Stenn P, Binkley K. Successful outcome in a patient with chemical sensitivity. Treatment with psychological desensitization and selective serotonin reuptake inhibitor. *Psychosomatics*. 1998;39:547-550.
- (118) Schmidt NB, McCreary BT, Trakowski JJ, Santiago HT, Woolaway-Bickel K, Ialongo N. Effects of cognitive behavioral treatment on physical health status in patients with panic disorder. *Behavior Therapy*. 2003;34:49-63.
Abstract: The relationship between panic disorder and nonpsychiatric medical illness is complex, but some evidence suggests that panic disorder increases risk for a variety of nonpsychiatric medical conditions. Given the demonstrated efficacy of cognitive behavioral therapy (CBT) for panic disorder, we were interested in evaluating the effects of CBT for panic disorder on nonpsychiatric medical symptoms among these patients. Patients were randomized to a 12-week group-administered CBT protocol (n = 22) or a delayed-treatment control (n = 24). Treated patients showed marked improvement in both anxiety symptoms and physical health symptom ratings that were evident at midtreatment and were maintained through a 6-month follow-up period. Despite comparable rates of change, changes in anxiety symptoms did not appear to mediate the relationship between treatment and improved physical health ratings. These findings indicate that CBT appears to have an immediate and long-term beneficial impact on physical health and that this effect is independent from its impact on anxiety symptoms
- (119) Kolk AM, Schagen S, Hanewald GJ. Multiple medically unexplained physical symptoms and health care utilization: outcome of psychological intervention and patient-related predictors of change. *J Psychosom Res*. 2004;57:379-389.
Abstract: OBJECTIVES: To test the effect of psychological intervention on multiple medically unexplained physical symptoms, psychological symptoms, and health care utilization in addition to medical care as usual. To identify patient-related predictors of change in symptoms and care utilization. METHODS: In a randomized controlled trial, subjects were assigned to one of two conditions: psychological intervention by a qualified therapist plus care as usual by a general practitioner (GP) or care as usual only. Participants (N=98) were administered a standardized interview and several outcome measures at intake and after 6 months and 12 months after intake. GPs rated medically unexplained and explained symptoms and consultations over a period of 1 1/2 years. RESULTS: ANOVAs for repeated measures showed that self-reported and GP-registered unexplained physical symptoms decreased from pretest to posttest to follow-up. Psychological symptoms and consultations decreased from pretest to posttest. GP-registered explained symptoms did not decrease. However, intervention and

control groups did not differ in symptom reduction. Path analysis revealed two paths to a decrease in self-reported unexplained physical symptoms: from more negative affectivity via more psychological attribution and more pretreatment anxiety, and from more somatic attribution via more psychological attribution and more pretreatment anxiety. CONCLUSION: Intervention and control groups did not differ in symptom reduction. Reduction of self-reported medically unexplained symptoms was well predicted by patient-related symptom perception variables, whereas the prediction of change in registered symptoms and consultations requires a different model

- (120) Saito M, Kumano H, Yoshiuchi K et al. Symptom profile of multiple chemical sensitivity in actual life. *Psychosom Med.* 2005;67:318-325.
Abstract: OBJECTIVE: This study was conducted to confirm the definition of multiple chemical sensitivity (MCS) in actual life: that multiple symptoms are provoked in multiple organs by exposure to, and ameliorated by avoidance of, multiple chemicals at low levels. We used the Ecological Momentary Assessment to monitor everyday symptoms and the active sampling and passive sampling methods to measure environmental chemical exposure. METHODS: Eighteen patients with MCS, diagnosed according to the 1999 consensus criteria, and 12 healthy controls participated in this study. Fourteen patients and 12 controls underwent 1-week measurement of physical and psychologic symptoms and of the levels of exposure to various chemicals. Linear mixed models were used to test the hypotheses regarding the symptom profile of MCS patients. RESULTS: Some causative chemicals were detected in 11 of 14 MCS patients. Two other patients did not report any hypersensitivity episodes, whereas passive sampling showed far less exposure to chemicals than control subjects. Another subject reported episodic symptoms but was excluded from the following analyses because no possible chemical was detected. Eleven of the 17 physical symptoms and all four mood subscales examined were significantly aggravated in the interview based on "patient-initiated symptom prompts." On the other hand, there were no differences in physical symptoms or mood subscales between MCS patients and control subjects in the interview based on "random prompts." CONCLUSIONS: MCS patients do not have either somatic or psychologic symptoms under chemical-free conditions, and symptoms may be provoked only when exposed to chemicals
- (121) Lacour M, Zunder T, Dettenkofer M, Schonbeck S, Ludtke R, Scheidt C. An interdisciplinary therapeutic approach for dealing with patients attributing chronic fatigue and functional memory disorders to environmental poisoning--a pilot study. *Int J Hyg Environ Health.* 2002;204:339-346.
Abstract: Nonspecific symptoms and a general feeling of ill health that is difficult to objectify are the commonest health problems with which patients present to an Environmental Medicine Outpatient Department (OPD). Of this group, a great proportion meets the classification criteria for Chronic Fatigue Syndrome (CFS) or Functional Memory Disorders in association with Idiopathic Chronic Fatigue (FMD-ICF). This is a longitudinal study of the OPD of Environmental Medicine, Freiburg University Hospital, Germany, to determine the feasibility and impact of an interdisciplinary therapeutic approach (self-help program, acupuncture, psychosomatic support by group interventions) in 8 patients with CFS, FMD-ICF, or CFS in association with self-reported Multiple Chemical Sensitivities (sr-MCS). The intervention took into consideration the patients' need for treatment of physical aspects of their disease. This is an important step to motivate patients into required psychosomatic support. Although none of the patients was willing to accept psychosomatic support or psychotherapy at study outset, acceptance of psychosomatic group interventions was high during the study course.

Additionally five patients started with personal counseling at the Psychosomatic Clinic, and, without feeling stigmatized, 4 patients started with specific psychotherapy. The patients' quality of life showed no increase after four months, but, as shown by the Sum-Score of SF-36, it had improved significantly at the end of the study, which covered eight months' treatment ($p = 0.015$). Two follow-up investigations showed that this improvement probably persisted in part (mainly in the dimensions mental health, social function, physical role function, and vitality). In conclusion our interdisciplinary therapeutic approach indicates successful treatment of patients attributing CFS, CFS/sr-MCS, and FMD-ICF to environmental poisoning. We now plan to conduct a randomized controlled trial in the future

- (122) Costa LG, Cole TB, Vitalone A, Furlong CE. Measurement of paraoxonase (PON1) status as a potential biomarker of susceptibility to organophosphate toxicity. *Clin Chim Acta*. 2005;352:37-47.

Abstract: Organophosphorus (OP) compounds are still among the most widely used insecticides, and their main mechanism of acute toxicity is associated with inhibition of acetylcholinesterase. Measurements of urine metabolites and of blood cholinesterase activity are established biomarkers of exposure to OPs and of early biological effects. In recent years, increasing attention has been given to biomarkers of susceptibility to OP toxicity. Here we discuss the polymorphisms of paraoxonase (PON1), a liver and serum enzyme that hydrolyzes a number of OP compounds, and its role in modulating the toxicity of OPs. We stress the importance of determining PON1 status, which encompasses the PON1192Q/R polymorphism (that affects catalytic ability toward different substrates) and PON1 levels (which are modulated in part by a C-108T polymorphism) over straight genotyping. Epidemiological studies on OP-exposed workers that include assessment of PON1 status to validate in human populations the role of PON1 as a determinant of susceptibility to OPs, as indicated by animal studies, are needed. Documentation of exposure and of early health effects would be most relevant to increase the predictive value of the test

- (123) Infante-Rivard C, Labuda D, Krajinovic M, Sinnett D. Risk of childhood leukemia associated with exposure to pesticides and with gene polymorphisms. *Epidemiology*. 1999;10:481-487. Abstract: We conducted a population-based case-control study of childhood acute lymphoblastic leukemia (ALL) to evaluate the risk posed by reported exposure to pesticides used in and around the home. We compared 491 cases 0-9 years of age to as many controls. We also conducted a case-only study on a subsample of 123 cases to evaluate gene-environment interaction between child genotype and maternal exposure during pregnancy as well as child exposure after birth. We used the polymerase chain reaction (PCR) approach to analyze polymorphisms in CYP1A1, CYP2D6, GSTT1, and GSTM1 genes, which encode enzymes involved in carcinogen metabolism. Indoor use of some insecticides by the owners and pesticide use in the garden and on interior plants, in particular frequent prenatal use, was associated with increased risks up to severalfold in magnitude. Interaction odds ratios were increased among carriers of the CYP1A1m1 and CYP1a1m2 mutations when mother during pregnancy or the child had been exposed to certain indoor insecticides. No such effects were observed in the presence of other tested polymorphisms

- (124) Binkley K, King N, Poonai N, Seeman P, Ulpian C, Kennedy J. Idiopathic environmental intolerance: increased prevalence of panic disorder-associated cholecystokinin B receptor allele 7. *J Allergy Clin Immunol*. 2001;107:887-890.

Abstract: BACKGROUND: A growing body of evidence suggests that idiopathic environmental intolerance (IEI) is a psychophysiological disorder with prominent features of

anxiety/panic and somatization, although proponents of a toxicogenic explanation claim, despite a lack of convincing evidence, that symptoms arise from exposure to otherwise nonnoxious environmental agents. Patient behaviour is characterized by strenuous avoidance of perceived triggers to the point of severe impairment of normal social and vocational functioning. IEI proponents claim that previous studies showing a high prevalence of psychopathology in patients with IEI and studies showing panic responses to known panicogenic challenges merely reflect the anxiety-producing result of living with IEI. **OBJECTIVE:** We explored whether IEI and panic disorder, personality traits, or both shared an underlying neurogenetic basis that would predate the anxiety of IEI symptomatology. The DNA of patients with IEI was examined for the presence of known panic disorder-associated cholecystokinin B (CCK-B) receptor alleles and for personality trait-associated dopamine D4 receptor polymorphisms. **METHODS:** Eleven patients with typical IEI symptoms were recruited and were individually matched to normal control subjects from an existing bank for age, sex, and ethnic background. Genomic DNA was extracted from peripheral blood samples. CCK-B and dopamine D4 receptor polymorphisms were examined by using standard PCR-based techniques. **RESULTS:** There was a significantly higher prevalence of the panic disorder-associated CCK-B receptor allele 7 in subjects with IEI (9/22 [40.9%]) compared with control subjects (2/22 [9.1%], $P = .037$). There was no difference in personality trait-associated polymorphisms of the gene encoding dopamine D4 receptor between patients and control subjects. **CONCLUSIONS:** These findings provide preliminary evidence that IEI and panic disorder share a common neurogenetic basis, which would predate the anxiety-producing effects of IEI symptoms. Further studies with larger samples are warranted, but these results support previous studies that suggest that panic disorder may account for much of the symptomatology in at least some cases of IEI and provide a basis for rational treatment strategies

- (125) Miresco MJ, Kirmayer LJ. The persistence of mind-brain dualism in psychiatric reasoning about clinical scenarios. *Am J Psychiatry*. 2006;163:913-918.
Abstract: **OBJECTIVE:** Despite attempts in psychiatry to adopt an integrative biopsychosocial model, social scientists have observed that psychiatrists continue to operate according to a mind-brain dichotomy in ways that are often covert and unacknowledged and suggest that the same intuitive cognitive schemas that people use to make judgments of responsibility lead to dualistic reasoning among clinicians. The goal of this study was to confirm these observations. **METHOD:** Self-report questionnaires were sent to the 270 psychiatrists and psychologists in the Department of Psychiatry at McGill University. In response to clinical vignettes, the participants rated the level of intentionality, controllability, responsibility, and blame attributable to the patients, as well as the importance of neurobiological, psychological, and social factors in explaining the patients' symptoms. **RESULTS:** A total of 136 faculty members (50.4%) responded, and 127 were included in the analysis. Factor analysis revealed a single dimension of responsibility regarding the patients' illnesses that correlated positively with ratings of psychological etiology and negatively with ratings of neurobiological etiology. Psychological and neurobiological ratings were inversely correlated. Multivariate analyses of variance supported these results. **CONCLUSIONS:** Mental health professionals continue to employ a mind-brain dichotomy when reasoning about clinical cases. The more a behavioral problem is seen as originating in "psychological" processes, the more a patient tends to be viewed as responsible and blameworthy for his or her symptoms; conversely, the more behaviors are attributed to neurobiological causes, the less likely patients are to be viewed as responsible and blameworthy

- (126) Grammer LC, Harris KE, Cugell DW, Patterson R. Evaluation of a worker with possible formaldehyde-induced asthma. *J Allergy Clin Immunol.* 1993;92:29-33.
Abstract: BACKGROUND: We describe the evaluation of a worker with clinical symptoms compatible with bronchospasm caused by formaldehyde exposure. METHODS: The worker was evaluated by means of enzyme-linked immunosorbent assay, cutaneous tests, and methacholine and formaldehyde inhalation challenges. The worker's serum was injected intradermally into the skin of a normal rhesus monkey to determine whether hypersensitivity could be transferred from human to primate. RESULTS: An enzyme-linked immunosorbent assay showed that the worker had positive IgE and IgG titers to formaldehyde-human serum albumin. The worker had a positive cutaneous test for formaldehyde-human serum albumin, and this cutaneous reactivity was transferred to a rhesus monkey through the worker's serum. The worker had a negative methacholine challenge at 25 mg/ml and negative formaldehyde inhalation challenges at 0.3, 1, 3, and 5 ppm for 20 minutes. It is possible that the worker would have had a positive result if a higher concentration of F were used for the challenge, but it is more probable that the worker's symptoms were not caused by immunologically mediated asthma. We have studied individuals exposed to formaldehyde, their clinical syndromes, and serologic results for a decade. This worker is the one subject with the most compatible history and immunology, but the worker had a negative challenge. CONCLUSION: Immunologically mediated asthma caused by formaldehyde is extremely rare, if it exists at all
- (127) Hasegawa M, Ohtomo M, Mita H, Akiyama K. [Clinical aspects of patients with MCS - from the standpoint of allergy]. *Arerugi.* 2005;54:478-484.
Abstract: BACKGROUND: "Sick House Syndrome" is thought to be an illness caused by indoor environments such as allergens, bacteria and chemical compounds. But it is not yet an established clinical entity. "Sick House Syndrome" overlaps in part with Multiple Chemical Sensitivity (MCS) whose symptoms are induced by very small amount of volatile chemical compounds. METHODS: We selected possible cases of MCS from patients who visited our specially built facility for "Sick House Syndrome" by tentative criteria as follow: (1) histories of chemical compounds exposure, (2) multi-organ symptoms, (3) exclusion of other disease(s) which may be responsible for symptoms, (4) chronic symptoms. Clinical aspects of the possible cases were examined. RESULTS: Fifty out of about 130 patients were the possible cases of MCS, 38 females and 12 males, aged 15 to 71 years old. Forty two out of 50 patients (84%) had a history and/or a complication of allergic diseases. This rate is much higher than the rate of prevalence of allergic diseases in Japanese population. Allergic rhinitis was the most popular allergic disease in the possible cases. Total IgE values were relatively low, 32 patients (64%) showed the IgE value below 200 IU/ml. No patients showed anti-formaldehyde IgE antibody. Decreased reactivity and decreased sensitivity of histamine release from peripheral blood were observed after challenge tests with chemical compounds. CONCLUSION: Allergic reactions can not be the causative mechanism(s) of the MCS, which is induced by multiple and different chemical compounds. Our results, however, suggest that patients having allergic diseases may be easily suffered from MCS or MCS may strengthen symptoms of allergic diseases
- (128) Campbell AW, Thrasher JD, Madison RA, Vojdani A, Gray MR, Johnson A. Neural autoantibodies and neurophysiologic abnormalities in patients exposed to molds in water-damaged buildings. *Arch Environ Health.* 2003;58:464-474.
Abstract: Adverse health effects of fungal bioaerosols on occupants of water-damaged homes and other buildings have been reported. Recently, it has been suggested that mold exposure causes neurological injury. The authors investigated neurological antibodies and neurophysiological abnormalities in patients exposed to molds at home who developed

symptoms of peripheral neuropathy (i.e., numbness, tingling, tremors, and muscle weakness in the extremities). Serum samples were collected and analyzed with the enzyme-linked immunosorbent assay (ELISA) technique for antibodies to myelin basic protein, myelin-associated glycoprotein, ganglioside GM1, sulfatide, myelin oligodendrocyte glycoprotein, alpha-B-crystallin, chondroitin sulfate, tubulin, and neurofilament. Antibodies to molds and mycotoxins were also determined with ELISA, as reported previously. Neurophysiologic evaluations for latency, amplitude, and velocity were performed on 4 motor nerves (median, ulnar, peroneal, and tibial), and for latency and amplitude on 3 sensory nerves (median, ulnar, and sural). Patients with documented, measured exposure to molds had elevated titers of antibodies (immunoglobulin [Ig]A, IgM, and IgG) to neural-specific antigens. Nerve conduction studies revealed 4 patient groupings: (1) mixed sensory-motor polyneuropathy (n = 55, abnormal), (2) motor neuropathy (n = 17, abnormal), (3) sensory neuropathy (n = 27, abnormal), and (4) those with symptoms but no neurophysiological abnormalities (n = 20, normal controls). All groups showed significantly increased autoantibody titers for all isotypes (IgA, IgM, and IgG) of antibodies to neural antigens when compared with 500 healthy controls. Groups 1 through 3 also exhibited abnormal neurophysiologic findings. The authors concluded that exposure to molds in water-damaged buildings increased the risk for development of neural autoantibodies, peripheral neuropathy, and neurophysiologic abnormalities in exposed individuals

- (129) Welch DA, Christenson D, Penley L, Chan P, Scoggins P, Shapiro S, Coryell M, Smith W, and O'Grady J. Letter from the National Treasury employees Union to Stephen L. Johnson, Administrator, U.S. Environmental Protection Agency. Public Employees for Environmental Responsibility . 24-5-2006. http://www.peer.org/docs/epa/06_25_5_union_ltr.pdf
Abstract: With regard to lack of neurotoxicity testing of 20 neurotoxic pesticides, which is not being carried out, "We Local Presidents of EPA Unions representing scientists, risk managers, and related staff, are writing to express our concern that EPA could betray the public trust by violating the intention of the Food Quality Protection Act (FQPA) to protect the Nation's infants, children, and susceptible subpopulations, unless the Agency adheres to principles of scientific integrity and sound science in the pesticide tolerance reassessments it is undertaking."
- (130) Anway MD, Skinner MK. Epigenetic Transgenerational Actions of Endocrine Disruptors. *Endocrinology*. 2006;147:s43-s49.
Abstract: Endocrine disruptors have recently been shown to promote an epigenetic transgenerational phenotype involving a number of disease states (e.g. male infertility). The anti-androgenic fungicide vinclozolin was found to act transiently at the time of embryonic sex determination to promote in the F1 generation a spermatogenic cell defect and subfertility in the male. When the animals were allowed to age up to 1 yr, a number of other disease states developed. This phenotype was transferred through the male germ line to all subsequent generations analyzed (F1-F4). The ability of an environmental factor (i.e. endocrine disruptor) to promote an epigenetic transgenerational phenotype impacts the potential hazards of environmental toxins, mechanisms of disease etiology, and evolutionary biology. The biological importance of the epigenetic actions of environmental agents is reviewed in the context of the primordial germ cell and development of epigenetic transgenerational phenotypes
- (131) Crews D, McLachlan JA. Epigenetics, Evolution, Endocrine Disruption, Health, and Disease. *Endocrinology*. 2006;147:s4-10.
Abstract: Endocrine-disrupting chemicals (EDCs) in the environment have been linked to human health and disease. This is particularly evident in compounds that mimic the effects of

estrogens. Exposure to EDCs early in life can increase risk levels of compromised physical and mental health. Epigenetic mechanisms have been implicated in this process. Transgenerational consequences of EDC exposure is also discussed in both a proximate (mechanism) and ultimate (evolution) context as well as recent work suggesting how such transmission might become incorporated into the genome and subject to selection. We suggest a perspective for exploring and ultimately coming to understand diseases that may have environmental or endocrine origins

- (132) Cecchini MA, Root DE, Rachunow JR, Gleb PM. Managing Chronic Illness in Patients. Health Status of Rescue Workers Improved by Sauna Detoxification. *Townsend Letter The Examiner of Alternative Medicine*. 2006.
Abstract: The improvements attained in almost 500 cases argue for broader implementation of the program, supported by additional evaluation and research efforts. That a large percentage of those affected by 9/11 exposures are not responding to existing treatments after more than four years; that the opportunity to improve the job fitness of first responders in one of the nation's most important cities exists; and that the possibility that syndromes being treated as "post traumatic stress" are in fact the result of toxin-induced damage - all this argues strongly for and adds urgency to this initiative.
- (133) Schnare DW, Ben M, and Shields MG. Body Burden Reductions of PCBS, PBBs and Chlorinated Pesticides in Human Subjects. *AMBIO A journal of the human environment* 13, 378-380. 1984. <http://www.rehabnz.co.nz/media2/ambio.pdf>
Abstract: With human exposure to environmental contaminants inevitable despite the best application of environmental laws and protection technologies, interest has grown in the potential to reduce the levels of contamination carried in the human host. This study demonstrates the promise of a comprehensive treatment for reduction of body burdens of polychlorinated and polybrominated biphenyls (PCB and PBB) and chlorinated pesticides. Adipose tissue concentrations were determined for seven individuals accidentally exposed to PBB. These patients underwent the detoxification treatment developed by Hubbard to eliminate fat-stored foreign compounds. Of the 16 organohalides examined, 13 were present in lower concentrations at post-treatment sampling. Seven of the 13 reductions were statistically significant; reductions ranged from 3.5 to 47.2 percent, with a mean reduction among the 16 chemicals of 21.3 percent (s.d. 17.1 percent). To determine whether reductions reflected movement to other body compartments or actual burden reduction, a post-treatment follow-up sample was taken four months later. Follow-up analysis showed a reduction in all 16 chemicals averaging 42.4 percent (s.d. 17.1 percent) and ranging from 10.1 to 65.9 percent. Ten of the 16 reductions were statistically significant. Future research stemming from this study should include further investigation of mobilization and excretion of xenobiotics in humans.
- (134) Younglai EV, Holloway AC, Foster WG. Environmental and occupational factors affecting fertility and IVF success. *Hum Reprod Update*. 2005;11:43-57.
Abstract: Reproductive function has been shown to be sensitive to changes in the physical, psychosocial and chemical environments. Although reproductive effects of occupational exposure to hazardous chemicals have been well documented in the literature, the potential effects of chemical contaminants at levels representative of contemporary exposures in the general population are much less certain. Evidence for adverse effects of exposure to environmental contaminants is more conclusive among the lower animals than for humans where considerable controversy remains. In addition to potential reproductive hazards of exposure to environmental contaminants, there is also evidence for adverse reproductive effects of the physical and psychosocial environments. In this review we focus on the difficulties

involved in linking exposure to putative hazardous substances in environmental and occupational settings to adverse reproductive outcomes, especially success of IVF procedures. We highlight the plausibility of adverse events through animal and cell studies and the application of these results to the interpretation of human data. We consider both the male and female partners since it is essentially their combined contributions of gametes which may be affected by chemicals, which lead to successful outcomes

- (135) Younglai EV, Foster WG, Hughes EG, Trim K, Jarrell JF. Levels of environmental contaminants in human follicular fluid, serum, and seminal plasma of couples undergoing in vitro fertilization. *Arch Environ Contam Toxicol*. 2002;43:121-126.
Abstract: Environmental chemicals are thought to adversely affect human reproductive function, however there are no studies that have explored the association between failed fertilization and exposure of both partners to environmental contaminants. Therefore, we collected blood and follicular fluid from the female partner and seminal plasma from the male partner of 21 couples attending an in vitro fertilization (IVF) program, in order to determine the extent of the existence of environmental chemicals in these fluids. Any relationship to the outcome of IVF was also considered. Sera and fluids were analysed for a variety of contaminants, including polychlorinated biphenyls, pesticides, cotinine, and the steroids progesterone and estradiol. Of the couples examined, 18 had fertilizations, three of whom became pregnant. There were no fertilizations in three other couples. The contaminants most frequently found in follicular fluid, more than 50% of the samples tested, were p,p'-DDE, mirex, hexachloroethane, 1,2,4-trichlorobenzene, PCB 49, PCB 153, and PCB 180. Cadmium was detected in eight of 21 (38.1%) samples of follicular fluid whereas cotinine was detected in 18 (85.7%). Residue levels of p,p'-DDE, endosulfan I, PCB 99, PCB 138, PCB 153, PCB 180 were quantified in more than 50% of the sera samples examined. Seminal plasma was relatively free of pollutants with mirex being the most frequently detected contaminant found in seven of 21 (33.3%) samples. Mirex could not be detected in the seminal plasma of the husbands whose partner's oocytes failed to fertilize whereas significant levels of mirex were found in the seminal plasma of all couples who had a pregnancy. Cadmium was also found in the follicular fluid of these pregnant subjects. No relationship was found between follicular fluid cotinine in pregnant and non-pregnant subjects. Where identical contaminants were found in both sera and follicular fluids, the levels were about twofold higher in serum and were positively correlated in both fluids. Fertilization was negatively correlated with serum and follicular fluid p,p'-DDE whereas pregnancy was positively correlated with follicular fluid PCB 49. These data reveal that more than 50% of the population of women attending a fertility program have had exposure to environmental chemicals sufficient to produce detectable concentrations in their serum and ovarian follicular fluid. Of the chemical contaminants detected in the serum and follicular fluid of these women, p,p'-DDE was the most frequently detected, had the highest residue levels, and was associated with failed fertilization
- (136) Swan SH. Semen quality in fertile US men in relation to geographical area and pesticide exposure. *Int J Androl*. 2006;29:62-68.
Abstract: We conducted the first US study to compare semen quality among study centres using standardized methods and strict quality control. We present data on semen quality in partners of 493 pregnant women recruited through prenatal clinics in four US cities during 1999-2001. Sperm concentration, semen volume and motility were determined at the centres and morphology was assessed at a central laboratory. While between-centre differences in sperm morphology and sample volume were small, sperm concentration and motility were significantly reduced in Columbia, MO (MO) relative to men in New York, NY, Minneapolis,

MN and Los Angeles, CA; total number of motile sperm was 113×10^6 in MO and 162, 201 and 196×10^6 in CA, MN and NY respectively. Differences among centres remained significant in multivariate models that controlled for abstinence time, semen analysis time, age, race, smoking, history of sexually transmitted disease and recent fever (all p-values <0.01). We hypothesized that poorer sperm concentration and motility in MO men relative to other centres might be related to agricultural pesticides that are commonly used in the mid-west. We investigated this hypothesis by conducting a nested case-control study within the MO cohort. We selected 25 men in this cohort for whom all semen parameters (concentration, % normal morphology and % motile) were low as cases and an equal number of men for whom all semen parameters were within normal limits as controls. We measured metabolites of eight non-persistent, current-use pesticides in urine samples the men had provided at the time of semen collection. Pesticide metabolite levels were elevated in cases compared with controls for the herbicides alachlor and atrazine, and for the insecticide diazinon (2-isopropoxy-4-methylpyrimidinol) (p-values for Wilcoxon rank test = 0.0007, 0.012, and 0.0004 for alachlor, atrazine and diazinon respectively). Men with higher levels of alachlor or diazinon were significantly more likely to be cases than men with low levels [odds ratios (OR) = 30.0, 16.7 for alachlor and diazinon respectively], as were men with atrazine over the limit of detection (OR = 11.3). These associations between current-use pesticides and reduced semen quality suggest that agricultural chemicals may have contributed to the reduced semen quality seen in fertile men from mid-Missouri

- (137) Arbuckle TE, Schrader SM, Cole D et al. 2,4-Dichlorophenoxyacetic acid residues in semen of Ontario farmers. *Reprod Toxicol.* 1999;13:421-429.
Abstract: Although paternal exposures to environmental toxicants probably play a role in adverse pregnancy outcomes, few data are available on the extent of this exposure. One semen and two 24-h urine samples were collected from 97 Ontario farmers who had recently used the phenoxy herbicides 2,4-D (2,4-dichlorophenoxyacetic acid) and/or MCPA ([4-chloro-2-methylphenoxy] acetic acid). Both samples were analyzed for 2,4-D using an immunoassay-based technique. Approximately 50% of the semen samples had detectable levels of 2, 4-D ($>$ or $=5.0$ ppb (ng/mL)). Semen levels of 2,4-D were correlated more closely with the second of the two urine samples. Although several studies have measured 2,4-D in the urine of applicators, this study is the first to attempt to measure 2,4-D levels in semen. As these pesticides can be excreted in the semen, they could be toxic to sperm cells and be transported to the woman and developing embryo/fetus. Further research is needed to understand how pesticide handling practices can affect semen pesticide residues and the relationship between the levels observed and reproductive health
- (138) Environmental Defence. Toxic Nation A report on pollution in Canadians. Environmental Defence . 2005.
http://www.environmentaldefence.ca/toxicnation/report/Rev_English%20Web.pdf available from <http://www.environmentaldefence.ca/toxicnation/resources/publications.htm#2>
- (139) Environmental Defence. Polluted Children Toxic Nation. A report on pollution in Canadian families. Environmental Defence . 2006.
http://www.environmentaldefence.ca/reports/PCTN_English%20Web.pdf available from <http://www.environmentaldefence.ca/reports/toxicnationFamily.htm>
- (140) Albertini R, Bird M, Doerrer N et al. The Use of Biomonitoring Data in Exposure and Human Health Risk Assessments. *Environ Health Perspect.* 2006;114:1755-1762.

Abstract: Biomonitoring uses analytic methods that permit the accurate measurement of low levels of environmental chemicals in human tissues. However, depending on the intended use, biomonitoring, like all exposure tools, may not be a stand-alone exposure assessment tool for some of its environmental public health uses. Although biomonitoring data demonstrate that many environmental chemicals are absorbed in human tissues, uncertainty exists regarding if and at what concentrations many of these chemicals cause adverse health outcomes. Moreover, without exposure pathway information, it is difficult to relate biomonitoring results to sources and routes of exposure and develop effective health risk management strategies. In September 2004, the Health and Environmental Sciences Institute, U.S. Environmental Protection Agency, Centers for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry, and International Council of Chemical Associations co-sponsored the International Biomonitoring Workshop, which explored the processes and information needed for placing biomonitoring data into perspective for risk assessment purposes, with special emphasis on integrating biomarker measurements of exposure, internal dose, and potential health outcome. Scientists from international governments, academia, and industry recommended criteria for applying biomonitoring data for various uses. Six case studies, which are part of this mini-monograph, were examined: inorganic arsenic, methyl eugenol, organophosphorus pesticides, perfluorooctanesulfonate, phthalates, and polybrominated diphenyl ethers. Based on the workshop and follow-up discussions, this overview article summarizes lessons learned, identifies data gaps, outlines research needs, and offers guidance for designing and conducting biomonitoring studies, as well as interpreting biomonitoring data in the context of risk assessment and risk management

- (141) Gibson, PR. Understanding & Accommodating People with Multiple Chemical Sensitivity in Independent Living. Independent living Research Utilization at TIRR . 2002.
http://www.geocities.com/mcs_canadian/gibson.html available from
<http://www.ilru.org/ilnet/files/bookshelf/mcs/mcs1.html>
- (142) Gilbert ME. Does the Kindling Model of Epilepsy Contribute to Our Understanding of Multiple Chemical Sensitivity? *Annals of the New York Academy of Sciences*. 2001;933:68-91.
- (143) Bell IR, Baldwin CM, Fernandez M, Schwartz GE. Neural sensitization model for multiple chemical sensitivity: overview of theory and empirical evidence. *Toxicol Ind Health*. 1999;15:295-304.
Abstract: This paper summarizes theory and evidence for a neural sensitization model of hyperresponsivity to low-level chemical exposures in multiple chemical sensitivity (MCS). MCS is a chronic polysymptomatic condition in which patients report illness from low levels of many different, structurally unrelated environmental chemicals (chemical intolerance, CI). Neural sensitization is the progressive host amplification of a response over time from repeated, intermittent exposures to a stimulus. Drugs, chemicals, endogenous mediators, and exogenous stressors can all initiate sensitization and can exhibit cross-sensitization between different classes of stimuli. The properties of sensitization overlap much of the clinical phenomenology of MCS. Animal studies have demonstrated sensitization to toluene, formaldehyde, and certain pesticides, as well as cross-sensitization, e.g., formaldehyde and cocaine. Controlled human studies in persons with self-reported CI have shown heightened sensitizability in the laboratory to nonspecific experimental factors and to specific chemical exposures. Useful outcome measures include spectral electroencephalography, blood pressure, heart rate, and plasma beta-endorphin. Findings implicate, in part, dopaminergic mesolimbic pathways and limbic structures. A convergence of evidence suggests that persons with MCS or with low-level CI

may share some characteristics with individuals genetically vulnerable to substance abuse: (a) elevated family histories of alcohol or drug problems; (b) heightened capacity for sensitization of autonomic variables in the laboratory; (c) increased amounts of electroencephalographic alpha activity at rest and under challenge conditions over time. Sensitization is compatible with other models for MCS as well. The neural sensitization model provides a direction for further systematic human and animal research on the physiological bases of MCS and CI

- (144) Sorg BA, Willis JR, See RE, Hopkins B, Westberg HH. Repeated low-level formaldehyde exposure produces cross-sensitization to cocaine: possible relevance to chemical sensitivity in humans. *Neuropsychopharmacology*. 1998;18:385-394.
Abstract: Sensitivity to chemicals in humans has been proposed to be an acquired disorder in which individuals become increasingly sensitive to chemicals in the environment. A possible link between the manifestation of psychiatric symptoms in individuals claiming sensitivity to chemicals was investigated based on a leading hypothesis put forth by Bell and co-workers (1992) to explain the amplification of symptoms after chemical exposure. The hypothesis is that chemical sensitivities may be akin to sensitization observed in rodents after repeated psychostimulants. Repeated exposure to psychostimulants enhances behavioral activity and the underlying neurochemical responses in specific limbic pathways; a similar sensitization of limbic pathways has been proposed to occur in individuals who become sensitive to chemicals. To test this hypothesis, female Sprague-Dawley rats were exposed to either air or formaldehyde (Form) for 1 h/day for 7 days or 20 days (5 days/week x 4 weeks). Two to 4 days after the last exposure, rats were given a cocaine challenge (= early withdrawal) followed by an additional cocaine challenge 4-6 weeks later (= late withdrawal). No differences in cocaine-induced locomotor activity were noted between groups after 7 days of exposure. However, after 20 days of exposure to Form, vertical activity was significantly elevated at both early and late withdrawal times. These studies demonstrate that behavioral sensitization occurs after long-term, but not short-term, low-level exposure to Form, and lends support to the limbic system sensitization hypothesis of sensitivity to chemicals in humans
- (145) Heuser G, Wu JC. Deep Subcortical (Including Limbic) Hypermetabolism in Patients with Chemical Intolerance: Human PET Studies. *Annals of the New York Academy of Sciences*. 2001;933:319-322.
- (146) Pall ML, Anderson JH. The vanilloid receptor as a putative target of diverse chemicals in multiple chemical sensitivity. *Arch Environ Health*. 2004;59:363-375.
Abstract: The vanilloid receptor (TRPV1 or VR1), widely distributed in the central and peripheral nervous system, is activated by a broad range of chemicals similar to those implicated in Multiple Chemical Sensitivity (MCS) Syndrome. The vanilloid receptor is reportedly hyperresponsive in MCS and can increase nitric oxide levels and stimulate N-methyl-D-aspartate (NMDA) receptor activity, both of which are important features in the previously proposed central role of nitric oxide and NMDA receptors in MCS. Vanilloid receptor activity is markedly altered by multiple mechanisms, possibly providing an explanation for the increased activity in MCS and symptom masking by previous chemical exposure. Activation of this receptor by certain mycotoxins may account for some cases of sick building syndrome, a frequent precursor of MCS. Twelve types of evidence implicate the vanilloid receptor as the major target of chemicals, including volatile organic solvents (but not pesticides) in MCS

- (147) Pall ML, Satterlee JD. Elevated Nitric Oxide/Peroxynitrite Mechanism for the Common Etiology of Multiple Chemical Sensitivity, Chronic Fatigue Syndrome, and Posttraumatic Stress Disorder. *Annals of the New York Academy of Sciences*. 2001;933:323-329.
- (148) Corrigan FM, MacDonald S, Brown A, Armstrong K, Armstrong EM. Neurasthenic fatigue, chemical sensitivity and GABA_A receptor toxins. *Med Hypotheses*. 1994;43:195-200.
Abstract: Following observation of fatigue syndromes in people who have been occupationally exposed to pesticides and insecticides which exert their toxicity through the GABA_A receptor, we have formulated the hypothesis that fatigue syndromes in general may be secondary to altered sensitivity of the GABA_A receptor. We discuss the possible involvement of organochlorine compounds which are widespread in the environment. Organophosphate compounds may have similar toxic effects through damaged cholinergic input to the dentate gyrus of the hippocampus where cholinergic and GABAergic transmission are closely linked
- (149) Overstreet DH, Djuric V. A Genetic Rat Model of Cholinergic Hypersensitivity: Implications for Chemical Intolerance, Chronic Fatigue, and Asthma. *Annals of the New York Academy of Sciences*. 2001;933:92-102.
- (150) Pall ML. NMDA sensitization and stimulation by peroxynitrite, nitric oxide, and organic solvents as the mechanism of chemical sensitivity in multiple chemical sensitivity. *FASEB J*. 2002;16:1407-1417.
Abstract: Multiple chemical sensitivity (MCS) is a condition where previous exposure to hydrophobic organic solvents or pesticides appears to render people hypersensitive to a wide range of chemicals, including organic solvents. The hypersensitivity is often exquisite, with MCS individuals showing sensitivity that appears to be at least two orders of magnitude greater than that of normal individuals. This paper presents a plausible set of interacting mechanisms to explain such heightened sensitivity. It is based on two earlier theories of MCS: the elevated nitric oxide/peroxynitrite theory and the neural sensitization theory. It is also based on evidence implicating excessive NMDA activity in MCS. Four sensitization mechanisms are proposed to act synergistically, each based on known physiological mechanisms: Nitric oxide-mediated stimulation of neurotransmitter (glutamate) release; peroxynitrite-mediated ATP depletion and consequent hypersensitivity of NMDA receptors; peroxynitrite-mediated increased permeability of the blood-brain barrier, producing increased accessibility of organic chemicals to the central nervous system; and nitric oxide inhibition of cytochrome P450 metabolism. Evidence for each of these mechanisms, which may also be involved in Parkinson's disease, is reviewed. These interacting mechanisms provide explanations for diverse aspects of MCS and a framework for hypothesis-driven MCS research
- (151) Gabriel G. Hans Selye: The Discovery of Stress. BrainConnection . 2006. available from <http://www.brainconnection.com/topics/?main=fa/selye#A1>
Abstract: As with so many wondrous discoveries of science and medicine, it was by chance that Hungarian-born Hans Selye (1907-1982) stumbled upon the idea of the General Adaptation Syndrome (G.A.S.), which he first wrote about in the British journal *Nature* in the summer of 1936. The G.A.S., alternately known as the stress syndrome, is what Selye came to call the process under which the body confronts "stress" (what he first called "noxious agents"). In the G.A.S., Selye explained, the body passes through three universal stages of coping. First there is an "alarm reaction," in which the body prepares itself for "fight or flight." No organism can sustain this condition of excitement, however, and a second stage of adaptation ensues (provided the organism survives the first stage). In the second stage, a resistance to the stress is

built. Finally, if the duration of the stress is sufficiently long, the body eventually enters a stage of exhaustion, a sort of aging "due to wear and tear."

"Stress," in Selye's lexicon, could be anything from prolonged food deprivation to the injection of a foreign substance into the body, to a good muscular workout; by "stress," he did not mean only "nervous stress," but "the nonspecific response of the body to any demand."

- (152) Nehlsen-Cannarella S, Fagoaga O, Folz J, Grinde S, Hisey C, Thorpe R. Fighting, fleeing and having fun: the immunology of physical activity. *Int J Sports Med.* 1997;18 Suppl 1:S8-21.:S8-21.

Abstract: Exercise places a spectrum of demands on the body, dependent on the form, intensity, and duration, which are super-imposed on a background of physiological and psychological factors peculiar to the host. Thus the net effect of these factors is both heterogeneous and complex. Studying the effects of exercise is dependent on an understanding of an elaborate network of interactions between the central nervous, endocrine, and immune systems that is yet to be understood. While investigators agree that immune suppression results from exhaustive exercise, opinions vary about its mechanism. Some of this is due to inter- and even intra-subject variation (perceptions, previous experience, gender, age, biological rhythms, other temporally related events, attributions, etc.), yet other is a result of differences in study design, parameters measured, methods and materials used, and a host of other variables. To achieve accord and to define the mechanisms leading to changes in health status, beneficial or harmful, that result from physical activity, we must strive to understand the complex network that exists in the psychoneuroendocrine immune system, design rigorous research models, standardize our methods, and offer sound hypotheses for future study. Lastly, investigations into exercise-induced immune alterations need to be conducted by multidisciplinary teams of individuals expert in each of the fields encompassed by this complex field of study. After offering some examples of the complex interactions between components of the psychoneuroendocrine immune axis, we discuss study design, caveats of laboratory methods, data reduction and interpretation, and a means of perhaps achieving our common goals in studying exercise immunology

- (153) Hiramoto RN, Rogers CF, Demissie S et al. Psychoneuroendocrine immunology: site of recognition, learning and memory in the immune system and the brain. *Int J Neurosci.* 1997;92:259-285.

Abstract: How the interaction between the brain and immune system takes place has not been clearly defined. Because multiple changes are occurring simultaneously in all organ systems (e.g., cardiovascular, gastrointestinal, reproductive, renal, respiratory, immune, CNS), how many single systems interacts with the brain becomes extraordinarily difficult to understand. The problem boils down to developing an approach that not only allows one to study the whole organism and define the mediators of the interacting systems, but also permit one to establish the connection and physiologic relevance of the responses that are being evaluated. Conditioning, a phenomenon made popular by the work of Pavlov (1906, 1927), may provide insight into the pathways of communication between the brain and possibly any organ system of the body. Conditioning allows one to separate the afferent from the efferent circuits. That is, signals from the immune system to the CNS (IS-->CNS) can be effectively separated from signals from the CNS to immune system (CNS-->IS). This permits one to study each pathway individually. Simple, single association trial models to condition fever, natural killer (NK) cell and cytotoxic lymphocyte (CTL) activities have been developed to evaluate the pathways. Single trial learning is not new. Pavlov has observed that "The electric buzzer set going before administration of food established a conditioned alimentary reflex after only a single

combination," whereas the reverse order of presentation failed to condition the animal (Pavlov 1927 p. 27). Thus, conditioning can be used to train the brain to activate the immune system and other organ systems participating in the response. During the course of the conditioned response, presumably the CNS via the hypothalamus integrates in a cohesive orderly fashion all input and output signals and coordinates the responses made by the brain to the organ systems. The odor of camphor, the conditioned stimulus (CS) can be associated with the response produced by an unconditioned stimulus (US). The unconditioned stimuli used are poly I:C to raise fever and nonimmunospesific NK cell activity or alloantigens to raise immunospesific CTL activity. The unconditioned stimulus serves only as a means to activate the immune system and unbalance the homeostasis so that a transient but new bidirectional communication loop can be established between the immune system and the CNS (IS \leftrightarrow CNS). The expression of the conditioned response (i.e., elevation of fever, NK cell, or CTL activity) induced with the CS (odor stimulus) is an outcome of neural activity (CNS \rightarrow IS). This infers that during conditioning, the signals generated by the CS and US imprints a neural pathway located within the central nervous system and leaves behind a CS/US memory of the association. The immune activity (NK cell or CTL activity) which is modulated indicate that the memory pathway was activated in the brain of the animal expressing the conditioned response. The immune cells that are modulated can be considered to be casual bystander cells. These cells however must be in the proper (ready) state of activation to receive salient signals from the brain. Along with changes in the indicator cell population, other complex physiological processes are altered by the brain via sympathetic and neuroendocrine pathways to raise the fever response. These observations suggest that the physiological changes which are being evaluated such as fever, NK cell or CTL activities or perhaps blood pressure, heart rate, fat metabolism, oxygen consumption serve only as indicators (readouts), and infer that the CNS has made a coordinated reply in response to the CS signal

- (154) Hiramoto RN, Solvason HB, Hsueh CM et al. Psychoneuroendocrine immunology: perception of stress can alter body temperature and natural killer cell activity. *Int J Neurosci.* 1999;98:95-129.
- Abstract: Psychoimmunology has been credited with using the mind as a way to alter immunity. The problem with this concept is that many of the current psychoimmunology techniques in use are aimed at alleviating stress effects on the immune system rather than at direct augmentation of immunity by the brain. Studies in animals provide a model that permits us to approach the difficulties associated with gaining an understanding of the CNS-immune system connection. A particular advantage of using animals over humans is that psychological and social contributions play a less prominent role for animals than for human subjects, since the animals are all inbred and reared under identical controlled conditions. If the insightful information provided by animal studies is correct, then psychotherapy for the treatment of diseases might be made more effective if some aspect of this knowledge is included in the design of the treatment. We emphasize conditioning as a regimen and an acceptable way to train the brain to remember an output pathway to raise immunity. We propose that a specific drug or perception (mild stress, represented by rotation, total body heating or handling) could substitute and kindle the same output pathway without the need for conditioning. If this view is correct, then instead of using conditioning, it may be possible to use an antigen to activate desired immune cells, and substitute a drug or an external environmental sensory stimulus (perception) to energize the output pathway to these cells. Alternatively, monitoring alterations of body temperature in response to a drug or perception might allow us to follow how effectively the brain is performing in altering immunity. Studies with animals suggest that there are alternative ways to use the mind to raise natural or acquired immunity in man

- (155) Marshall LM, Bested A, Bray RI. Tools to treat Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity. *The Canadian Journal of CME*. 2004;56-65.
- (156) Ontario College of Family Physicians. Case Criteria Checklists (Chronic Fatigue Syndrome, Fibromyalgia, Multiple Chemical Sensitivity). OCFP . 2003. available from <http://www.ocfp.on.ca/english/ocfp/communications/publications/default.asp?s=1>
- (157) Soden SE and Lowry JA. Provocative urine excretion of heavy metals using meso-2,3-dimercaptosuccinic acid (DMSA) in children with autism. Children's Mercy Hospitals & Clinics (Bridge Grant) . 2006. available from http://www.cureautismnow.org/site/c.bhLOK2PILuF/b.1452295/k.9511/Sarah_E_Soden_and_Jennifer_A_Lowry_Childrens_Mercy_Hospitals_Clinics_Bridge_Grant.htm
 Abstract: The investigators propose measurement of urinary mercury, lead, cadmium, arsenic, and aluminum prior to and during a 24 hour provocative urine excretion study; comparing children with autism to non-autistic age matched controls. For the provoked excretion, we will use a heavy metal chelator meso-2,3-dimercaptosuccinic acid (DMSA). Our goals are to document difference that may exist between the two groups, to direct follow-up study, and to collect normative data for provocative urinary excretion of these environmental toxins.
- (158) Krop JJ. *Healing the planet one patient at a time A primer in environmental medicine*. Alton ON Canada: KOS Publishing Inc.; 2002.
- (159) Bested AC, Logan AC, Howe R. *Hope and help for chronic fatigue syndrome and fibromyalgia*. Cumberland House Publishing, Nashville, Tennessee, USA; 2006.
- (160) Bray R, Coates D, Marshall LM, Rizvi K, and Masson C. Water contaminants: Health effects on children. Children's Health and the Environment: Building capacity for policy development and facilitating policy change, A report to the Canadian Institute for Child Health. 2003. Canadian Institute for Child Health.
- (161) Rashid M, Cranney A, Zarkadas M et al. Celiac disease: evaluation of the diagnosis and dietary compliance in Canadian children. *Pediatrics*. 2005;116:e754-e759.
 Abstract: OBJECTIVES: We sought to characterize the clinical features at presentation as well as the associated disorders, family history, and evaluation of compliance with a gluten-free diet in children with celiac disease from across Canada. STUDY DESIGN: All members (n = 5240) of the Canadian Celiac Association were surveyed with a questionnaire. Of the 2849 respondents with biopsy-confirmed celiac disease, 168 who were < 16 years old provided the data reported here. RESULTS: The mean age when surveyed was 9.1 +/- 4.1 years, and 58% were female. Median age at diagnosis was 3.0 years with a range of 1 to 15 years. Presenting symptoms included abdominal pain (90%), weight loss (71%), diarrhea (65%), weakness (64%), nausea/vomiting (53%), anemia (40%), mood swings (37%), and constipation (30%). Almost one third of families consulted > or = 2 pediatricians before confirmation of the diagnosis. Before the recognition of celiac disease, other diagnoses received by these children included anemia (15%), irritable bowel syndrome (11%), gastroesophageal reflux (8%), stress (8%), and peptic ulcer disease (4%). A serological test was performed to screen for celiac disease in 70% of those in this population. Eight percent had either type 1 diabetes mellitus or a first-degree relative with celiac disease. Almost all respondents (95%) reported strict adherence to a gluten-free diet, and 89% noted improved health. Reactions after accidental gluten ingestion developed in 54% of the children between 0.5 and 60 hours after ingestion with a

median of 2.0 hours. Reactions included abdominal discomfort (87%), diarrhea (64%), bloating (57%), fatigue (37%), headache (24%), and constipation (8%), and most displayed > 1 symptom. Although most adjusted well to their disease and diet, 10% to 20% reported major disruptions in lifestyle. Twenty-three percent felt angry all or most of the time about following a gluten-free diet. Only 15% avoided traveling all or most of the time, and during travel, 83% brought gluten-free food with them all of the time. More than half of the families avoided restaurants all or most of the time. Twenty-eight percent of the respondents found it extremely difficult to locate stores with gluten-free foods, and 27% reported extreme difficulty in finding gluten-free foods or determining if foods were free of gluten. Sixty-three percent of the respondents felt that the information supplied by the Canadian Celiac Association was excellent. Gastroenterologists provided excellent information to 44%, dietitians to 36%, and the family physician to 11.5%. When asked to select 2 items that would improve their quality of life, better labeling of gluten-containing ingredients was selected by 63%, more gluten-free foods in the supermarket by 49%, gluten-free choices on restaurant menus by 49%, earlier diagnosis of celiac disease by 34%, and better dietary counseling by 7%. CONCLUSIONS: In Canada, children with celiac disease present at all ages with a variety of symptoms and associated conditions. Delays in diagnosis are common. Most children are compliant with a gluten-free diet. A minority of these children experience difficulties in modifying their lifestyles, and gluten-free foods remain difficult to obtain

- (162) Accomando S, Cataldo F. The global village of celiac disease. *Dig Liver Dis.* 2004;36:492-498. Abstract: In the last years our knowledge on epidemiology of celiac disease has increased: there is a wide spectrum of its clinical presentation (classical, atypical, silent and latent forms of celiac disease), and of its pathological mucosal intestinal features, which range from early and mild pictures to severe villous atrophy (Marsh stages). In addition, a strong genetic component, associated with the susceptibility to the disease (HLA and non HLA genes), has been found. This knowledge, together with the availability of new high sensitive and specific serological tests (antigliadin, antiendomysium and antitransglutaminase antibodies), has led us to the realization that celiac disease is the most common food intolerance in the world, involving genetically predisposed individuals consuming gluten-containing cereals in their diet. So, today it is well known that celiac disease is a common disorder not only in Europe but also in populations of European ancestry (North and South Americas, Australia), in North Africa, in the Middle East and in South Asia, where until a few years ago it was historically considered extremely rare. Therefore, celiac disease is spread worldwide as in a common "Global Village", and greater levels of awareness and attention on gluten intolerance are needed, both in the Old and in the New World
- (163) Kitts D, Yuan Y, Joneja J et al. Adverse reactions to food constituents: allergy, intolerance, and autoimmunity. *Can J Physiol Pharmacol.* 1997;75:241-254. Abstract: Food allergies and intolerance represent important health concerns to consumers who are predisposed to these illnesses. Unlike many current food safety issues, food sensitivities are complicated by both complex and multiple individual adverse reactions, which can vary from emotional to pathophysiological ailments. In some instances, the underlying mechanisms that result in the development of food allergies or intolerance have marked differences but produce common symptoms. The present-day diagnosis of these disorders can be impeded by intrinsic limitations in generating accurate information from patient history and biochemical, physicochemical, and immunochemical tests. Oral challenge tests represent effective methods for confirming and testing food allergens and food intolerance; however, these procedures are often restricted to clinical trials. It is important to be able to distinguish among food allergy,

intolerance, and autoimmune disease in the management of these disorders. The role of food in the development of autoimmune disease may be exemplified by celiac disease, a food-induced enteropathy, requiring exposure to prolamins in wheat, rye, and barley. Various wheat and soy protein sources, including the soy protein isolates used to make infant formulas, have been related to juvenile or insulin-dependent diabetes mellitus (IDDM), a common chronic disease of childhood. Employing food process technologies to eliminate food constituents with potential for intolerance in some individuals is a potentially viable approach for reducing risk to food-related disorders. Finally, the development of food labelling regulations that require the identification of potential food allergens or agents for intolerance in the ingredient declaration on prepackaged food is a positive step toward the prevention of severe adverse reactions in hypersensitive individuals

- (164) Logan AC, Wong C. Chronic fatigue syndrome: oxidative stress and dietary modifications. *Altern Med Rev.* 2001;6:450-459.

Abstract: Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear; however, a number of recent studies have shown oxidative stress may be involved in its pathogenesis. The role of oxidative stress in CFS is an important area for current and future research as it suggests the use of antioxidants in the management of CFS. Specifically, the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, and Vaccinium myrtillus (bilberry) may be beneficial. In addition, research on food intolerance is discussed, since food intolerance may be involved in CFS symptom presentation and in oxidation via cytokine induction. Finally, recent evidence suggests celiac disease can present with neurological symptoms in the absence of gastrointestinal symptoms; therefore, celiac disease should be included in the differential diagnosis of CFS

- (165) Chisolm JJ, Jr. Safety and efficacy of meso-2,3-dimercaptosuccinic acid (DMSA) in children with elevated blood lead concentrations. *J Toxicol Clin Toxicol.* 2000;38:365-375.

Abstract: OBJECTIVE: To evaluate the safety and efficacy of meso-2,3-dimercaptosuccinic acid in the treatment of children with lead toxicity. DESIGN: This was an open-label study in 59 children 12-65-months old, with pretreatment whole-blood lead levels of 25-66 microg/dL, who received 116, 26-28 day courses of oral dimer-captosuccinic acid, while residing either in the Pediatric Clinical Research Unit of the Johns Hopkins Hospital or in lead-safe housing during the outpatient portion of the study. RESULTS: All, who completed the study, showed sharp decreases in blood lead concentration during therapy, but 2-3 weeks following completion of drug therapy, blood lead concentration rebounded to an average of 58% (23 microg Pb/dL of whole blood) of their average pretreatment blood lead concentration (40 microg Pb/dL of whole blood). There were no adverse reactions attributable to dimercaptosuccinic acid; however, 2 of the 59 patients were reexposed to defective lead paint and experienced sharp increases in blood lead concentration while on therapy. In one instance, the child's blood lead concentration increased from 20 to 90 microg Pb/dL whole blood in 1 week. Other unexpected events were discussed in the text. CONCLUSIONS: Dimercaptosuccinic acid is apparently safe and does mobilize lead into the urine, but not the essential metals, zinc and copper. Reexposure is always a danger; therefore, all children, while on therapy, should be monitored for their blood lead concentration at weekly intervals during and immediately after therapy. No conclusions can be drawn from this study regarding long-term beneficial effects, if any, of this drug on late neurocognitive outcome

- (166) National Institutes of Health Clinical Center. An Investigation of the Efficacy of Mercury Chelation as a Treatment for Autism Spectrum Disorder. National Institutes of Health . 2006. <http://www.clinicaltrials.gov/ct/show/NCT00376194?order=1>
Abstract: Chelation of metals is widely used in the community to treat individuals with Autism Spectrum Disorder (ASD), with some surveys estimating that 1 in 12 children with autism have undergone chelation. This widespread use reflects the hypothesis that many cases of ASD are caused by exposure to thimerosal, an ethylmercury-based compound used previously in the US as a vaccine preservative for routine childhood immunizations. The prevalent use of chelation therapy stands in stark contrast with the lack of scientific or clinical evidence of efficacy, and creates a public health imperative for empiric data. Thus we propose a controlled trial of the effects of chelation on the core behavioral symptoms and overall functioning of children with ASD. The present investigation is a double-blind, randomized placebo-controlled study of the oral chelating agent meso-2,3-dimercaptosuccinic acid (DMSA; succimer) among 120 children, ages four to ten years, who meet criteria for ASD. Pre- and post-treatment behavioral ratings will be used to evaluate the efficacy of chelation. In addition, children will undergo comprehensive medical history, physical examination and laboratory analyses. Our objective is to quantify differences in behavioral functioning between the chelation treatment group and the placebo control group. Analysis of mercury levels before and during the course of treatment will be used to confirm the expected DMSA-induced excretion of mercury and to identify differences among children in the extent of excretion. Our primary hypothesis is that, on average and relative to the control group, children with ASD who undergo chelation with DMSA will show greater improvements in communication and social behavior.
- (167) Australian Human Rights and Equal Opportunity Commission. Advisory Notes on Access to Premises. Australian Human Rights and Equal Opportunity Commission . 2006. available from http://www.hreoc.gov.au/disability_rights/standards/Access_to_premises/premises_advisory.html
Abstract: There is a growing number of people affected by sensitivity to chemicals used in the building, maintenance and operation of premises. This can mean that premises are effectively inaccessible to people with chemical sensitivity. People who own, lease, operate and manage premises should consider the following issues to eliminate or minimise chemical sensitivity reactions in users:
- the selection of building, cleaning and maintenance chemicals and materials, in accordance with relevant environmental and occupational health and safety regulations and established standards;
 - provision of adequate ventilation and ensuring all fresh air intakes are clear of possible sources of pollution such as exhaust fumes from garages;
 - minimising use of air fresheners and pesticides.
- (168) State of California - State and Consumer Services Agency. Building Standards Bulletin 2004-01. State of California - State and Consumer Services Agency . 11-4-2004. http://www.bsc.ca.gov/cd_qustns/documents/CBSC_bulletin2004-01.pdf
Abstract: 1117B.5.12.2 Conditions of Use. Use of the cleaner-air symbol is voluntary. The Clean Air Symbol shall be permitted for use to identify a path of travel, and a room or a facility when the following is met:
1. Floor or wall coverings, floor or wall covering adhesives, carpets, or formaldehyde-emitting particleboard cabinetry, cupboards, or doors have not been installed or replaced in the previous 12 months.
 2. Incandescent lighting provided in lieu of fluorescent or halogen lighting, and electrical

systems and equipment shall be operable by or on behalf of the occupant or user of the room, facility, or path of travel.

3. Heating, ventilation, air conditioning and their controls shall be operable by or on behalf of the occupant or user.

4. To maintain "Cleaner-Air" designation, only non-irritating, non-toxic products will be used in cleaning, maintenance, disinfection, pest management, or for any minimal touch-ups, which are essential for occupancy of the area. Deodorizers or Fragrance Emission Devices and Systems (FEDS) shall not be used in the designated area. Pest control practices for Cleaner-Air areas shall include the use of bait stations using boric acid, sticky traps, and silicon caulk for sealing cracks and crevices. Areas shall be routinely monitored for pest problems. Additional non-toxic treatment methods, such as temperature extremes for termites, may be employed in the event of more urgent problems. These pest control practices shall not be used 48 hours prior to placement of the sign and the facility shall be ventilated with outside air for a minimum of 24-hours following use or application.

5. Signage shall be posted requesting occupants or users not to smoke or wear perfumes, colognes, or scented personal care products. Fragranced products shall not be used in the designated Cleaner-Air room, facility, or path of travel.

6. A log shall be maintained on site, accessible to the public either in person or by telephone, email, Fax, or other accessible means as requested. One or more individuals shall be designated to maintain the log. The log shall record any product or practice used in the Cleaner-Air designated room, facility, or path of travel, as well as scheduled activities, which may impact the Cleaner-Air designation. The log shall also include the product label as well as the material Safety Data Sheets (MSDS).

1117B.5.12.3 Removal of symbol. If the path of travel, room and/or facility identified by the Cleaner Air Symbol should temporarily or permanently cease to meet the minimum conditions as set forth above, the Cleaner Air Symbol shall be removed and shall not be replaced until the minimum conditions are again met.

- (169) National Institute of Building Sciences. IEQ Indoor Environmental Quality. 2005. National Institute of Building Sciences USA. http://ieq.nibs.org/ieq_project.pdf available from <http://ieq.nibs.org/index.php>

Abstract: The overall objectives of this project were to establish a collaborative process among a range of stakeholders to recommend practical, implementable actions to both improve access to buildings for people with MCS and EMS while at the same time raising the bar and improving indoor environmental quality to create healthier buildings for the entire population. This IEQ project supports and helps achieve the goals of the Healthy Buildings, Healthy People project, which acknowledges that "We will create indoor environments that are healthier for everyone by making indoor environments safer for the most vulnerable among us, especially children." The recommendations in this report are only a first step toward the action plan envisioned by the Access Board. It is recommended that a follow-on project organize and convene one, or more, workshops to deliberate the issues and recommendations in this report. It is also recommended that a project be organized to develop a single guidelines document. Such guidelines would be built on refinement and coordination of the recommendations of the Design & Construction and Products & Materials committees in this report. This same, or a separate project, should develop new building code provisions to accelerate the implementation of improved IEQ. Lastly, it is recommended that a project be organized to develop guidelines for the design of an "ideal space" for people with MCS and EMS. The recommended follow-up projects should involve collaborative effort and funding from a range of organizations across the building community; e.g., American Institute of Architects (AIA), Associated General

Contractors of America (AGC), Building Owners & Managers Association International (BOMA), American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE), Environmental Protection Agency (EPA), and, of course, the Access Board.

- (170) National Research Council. Canada's Code Development System. National Research Council . 29-1-2002. http://www.nationalcodes.ca/ccbfc/ccds_e.pdf available from http://www.nationalcodes.ca/ccbfc/ccds_e.pdf

Abstract: Canada's centralized system for model code development and maintenance began in the 1930s. The first edition of the National Building Code was published in 1941. Subsequent adoption of the model national building, plumbing, and fire codes by the provinces and territories has resulted in a progressive system that is responsive to new construction products and techniques.

The Canadian Commission on Building and Fire Codes (CCBFC), funded by code sales and the National Research Council, is responsible for developing and updating six model national codes. It oversees the work of nine committees and several task groups involving as many as 300 members. The system is structured such that it is the members of the committees who establish the content of the model codes. Member expertise from industry, the regulatory community and general interest groups is balanced to ensure that all relevant sectors and geographical areas of the country are represented. These committees are administratively and technically supported by the Canadian Codes Centre of the Institute for Research in Construction at the National Research Council.

- (171) Department of Health. Proposed residential indoor air quality guideline for moulds. Canada Gazette . 13-12-2006. available from <http://canadagazette.gc.ca/partI/2006/20061223/html/notice-e.html>

Abstract: Pursuant to subsection 55(3) of the Canadian Environmental Protection Act, 1999, the Minister of Health hereby gives notice of a proposed residential indoor air quality guideline for moulds. After reviewing the most recent scientific evidence regarding moulds and its effects on health, the Minister recommends

* to control humidity and diligently repair any water damage in residences to prevent mould growth; and

* to clean thoroughly any mould growing in residential buildings.

These recommendations apply regardless of the mould species found to be growing in the building.

Any person may, within 60 days after publication of this notice, file with the Minister of Health written comments on the proposed guidelines. All written comments will be made available upon request to all interested parties. All comments, requests for copies of the proposal, and information requests must cite the Canada Gazette, Part I, and the date of publication of this notice and be sent to the Air Health Effects Division, Health Canada, 269 Laurier Avenue W, 3rd Floor, PL 4903C, Ottawa, Ontario K1A 0K9, 613-957-1876 (telephone), 613-954-7612 (fax), air@hc-sc.gc.ca (email).

December 13, 2006

PAUL GLOVER

Director General

Safe Environments Programme

On behalf of the Minister of Health

- (172) Canadian Construction Association. CCA 82 - Mould Guidelines for the Canadian Construction Industry. 2004. <http://www.cca-acc.com/documents/electronic/cca82/cca82.pdf> available from

<http://www.cca-acc.com/mould/>

Abstract: CCA is proud to release its newest guide - CCA 82 - Mould Guidelines for the Canadian Construction Industry. This document has been produced by an Expert Task Force of some 20 representatives representing a wide range of disciplines. The Task Force was Chaired by Lionel Neveu, Director of Safety and Environment for PCL Constructors.

The Guide offers practical advice on mould-related issues (legal, insurance, and health considerations). It also offers helpful information on how to minimize its presence, identify and measure it, and step-by-step instructions on remediation.

- (173) Ontario Association of Architects. OAA Mould Control Practice Guide. Ontario Architects' Association . 2003. available from <http://www.oaa.on.ca/client/oa/OAAHome.nsf/PracticeBulletinByDate/714B32234DE278EB85256DAB00677847?Opendocument>
- Abstract: Mould control is not about selecting materials or applying biocides. Mould spores exist everywhere. Hence, mould control is primarily about controlling moisture to levels and durations appropriate for the material used. The general strategy is to construct and operate buildings in such a way that materials do not get wet enough to support mould growth or to ensure that those materials that get wet will dry quickly and do not provide sufficient food value to support mould growth.
- Most mould problems can be dealt with in a straightforward manner. Testing is rarely required or useful. Stop the mould from growing, remove it, and make sure it does not grow back by removing moisture sources, nutrients, or both. If the mould infestation is large or occupants are reporting health effects, one should act more quickly and firmly than if it is a small growth and the occupants are healthy. Mould remediation should follow the available guidelines. Identification, followed by removal or control of the moisture source that caused the problem, must be part of any remediation.
- Mould control should be considered in all phases of building design, construction, maintenance, and operation. In most cases where moisture is controlled, mould growth will not be a problem. Good moisture control strategies are described in the OAA Rain Penetration Control Practice Guide, CMHC Best Practice Guides, and other moisture control handbooks.
- This Guide cannot comprehensively cover all that is required, but it aims to provide an overview and background that will allow a skilled practitioner to avoid growth of damaging mould. Although the Guide's scope is broad, it does not cover the special needs of hypersensitive, highly allergic, or immuno-compromised occupants. A higher standard may be required for these special situations
- (174) World Health Organization Regional Office for Europe Copenhagen. Air Quality Guidelines for Europe . WHO Regional Publications, European Series, No.91 [Second Edition]. 2006. <http://www.euro.who.int/document/e71922.pdf>
- (175) Won, D., Magee, R. J., Yang, W., Luszyk, E., Nong, G., and Shaw, C. Y. A Material emission database for 90 target VOCs. National Research Council Canada . 2005. <http://irc.nrc-cnrc.gc.ca/pubs/fulltext/nrcc48314/nrcc48314.pdf>
- (176) Shaw, C. Y., Won, D., and Reardon, J. Managing Volatile Organic Compounds and Indoor Air Quality in Office Buildings – An Engineering Approach. RR-205. 2005. <http://irc.nrc-cnrc.gc.ca/pubs/rr/rr205/rr205.pdf> available from <http://irc.nrc-cnrc.gc.ca>

Abstract: This report gives a brief overview of various parameters affecting IAQ. It also provides some practical recommendations for maintaining good IAQ with a focus on

- (177) Apte MG, Fisk WJ, Daisey JM. Associations between indoor CO₂ concentrations and sick building syndrome symptoms in U.S. office buildings: an analysis of the 1994-1996 BASE study data. *Indoor Air*. 2000;10:246-257.

Abstract: Higher indoor concentrations of air pollutants due, in part, to lower ventilation rates are a potential cause of sick building syndrome (SBS) symptoms in office workers. The indoor carbon dioxide (CO₂) concentration is an approximate surrogate for indoor concentrations of other occupant-generated pollutants and for ventilation rate per occupant. Using multivariate logistic regression (MLR) analyses, we evaluated the relationship between indoor CO₂ concentrations and SBS symptoms in occupants from a probability sample of 41 U.S. office buildings. Two CO₂ metrics were constructed: average workday indoor minus average outdoor CO₂ (dCO₂, range 6-418 ppm), and maximum indoor 1-h moving average CO₂ minus outdoor CO₂ concentrations (dCO₂MAX). MLR analyses quantified dCO₂/SBS symptom associations, adjusting for personal and environmental factors. A dose-response relationship ($p < 0.05$) with odds ratios per 100 ppm dCO₂ ranging from 1.2 to 1.5 for sore throat, nose/sinus, tight chest, and wheezing was observed. The dCO₂MAX/SBS regression results were similar

- (178) Won, D., Luszyk, E., and Shaw, C. Y.

Target VOC List. National Research Council Canada . 2005. <http://irc.nrc-cnrc.gc.ca/pubs/rr/rr206/rr206.pdf> available from <http://irc.nrc-cnrc.gc.ca>

Abstract: A list of 90 compounds was compiled as a guide to identify and quantify specific chemicals emitted from building materials. The chemicals on the target VOC list include compounds that are: 1) known or suspected to have health or irritation concerns; 2) known to be emitted from the tested building materials; and 3) often found in indoor air. This list originally consisted of 120 compounds that are abundant indoors and that are emitted from building materials. It was refined, in consultation with the project's Health and End-User Advisory Committee (HEUAC), based on existing lists compiled by national and international organizations out of concerns on human health. The IRC target VOC list will be used to guide the identification and quantification of the chemical emitted from the building materials tested under the Phase 2 of the Material Emissions and Indoor Air Quality Modelling project. Forty-two of the 48 building material tests complete in Phase 1 of the project were also reanalysed to cover all chemicals on this target list (six had used BC/FID, making re-analysis impractical).

- (179) Environment Canada. The Need for Immediate Action - Canada's New Clean Air Regulatory Agenda - Background. The Green Lane™, Environment Canada's World Wide Web site . 19-10-2006. available from http://www.ec.gc.ca/press/2006/061019-3_b_e.htm

Abstract: Emissions from Consumer and Commercial Products

Regulations limiting Volatile Organic Compound (VOC)¹ content in: architectural, industrial and maintenance coatings; consumer products; and automobile refinishing coatings (together, paints, cosmetics and cleaning products account for about 18% of VOC emissions in Canada). Regulations to reduce VOC emissions from other consumer and commercial products, including regulations limiting VOC content in additional products such as portable fuel containers; and new strategies and instruments for reducing VOC emissions from printing, aerospace and automotive manufacturing sectors.

- (180) Lindblad-Toh K. Genome sequencing Three's company. *Nature*. 2004;428:475-476.

- (181) ASHRAE Board of Directors. Indoor Air Quality. American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. 1791 Tullie Circle, NE • Atlanta, Georgia 30329-2305 • (404) 636-8400 • fax: (404) 321-5478 • www.ashrae.org . 10-2-2005.

Abstract: People in buildings frequently report discomfort, building related illness, and other symptoms that occupants believe are caused by the indoor environment (e.g., sick building syndrome [SBS]). Temperature, humidity, drafts and a wide range of indoor air pollutants: organic and inorganic gases, infectious microorganisms, other biological agents, and nonbiological particles and fibers, are among indoor environmental factors implicated in occupant discomfort or illness reports. Sources of indoor air pollutants include building materials; materials used inside buildings (e.g., furnishings, cleaning products, paper); combustion appliances; office, HVAC and other equipment; tobacco smoking; people and their personal care products; the soil, vegetation and the outdoor air. Some building components may become pollutant sources through moisture incursion, accumulation of deposited particles or gases, or normal usage and maintenance. IAQ is a multidisciplinary endeavor; therefore, good communication and cooperation must be established among professionals who share responsibility for building environments. These professionals include architects, designers, builders, engineers, maintenance and custodial staff, facility managers, and, where appropriate, medical and environmental health professionals. Good communication and cooperation must be also established with building occupants, the subject of all IAQ efforts.

Further, ASHRAE recommends:

1. ASHRAE Standards 62.1 and 55 as the two major United States (U.S.) national guidelines on indoor thermal and IAQ management.
2. Expanded public and private support for research on IAQ and its effects on people because ASHRAE recognizes that there remains a significant need for continuing research on the causes, health effects, economic importance and solutions of IAQ problems.
3. Continued government support for IAQ-related education and implementation programs because ASHRAE recognizes that widespread implementation of available IAQ knowledge, technologies and practices can significantly improve indoor environments, comfort and public health.
4. Continued research on building energy efficiency and IAQ, which are interrelated but not incompatible.

ASHRAE will:

1. Continue to influence building design, operation and maintenance, which affect IAQ.
2. Continue to improve ASHRAE Standards 62.1 and 55 and promote their broad acceptance and implementation.
3. Support relevant research on ASHRAE Standards 62.1 and 55.
4. Continue educational IAQ programs for its members and all who are involved in the multiple aspects of IAQ.
5. Continue to support communication and information exchange among all disciplines that contribute to the study and improvement of IAQ.

- (182) Kilburn KH. Indoor air effects after building renovation and in manufactured homes. *Am J Med Sci.* 2000;320:249-254.

Abstract: **PROBLEM:** The objective was to measure and compare the neurobehavioral and respiratory effects of exposures to indoor air in people living in manufactured homes and occupying buildings during renovation and compare them with effects on subjects exposed to formaldehyde at work. **METHODS:** Ten people living in manufactured homes and 10 people exposed to chemicals during renovation of their offices or homes had measurements made of

balance, visual fields, reaction time, hearing, grip strength, and vibration sense. Psychological measurements included cognition, recall, perceptual motor speed, long-term memory, and mood states. RESULTS: Exposures to indoor air were associated with abnormal simple and choice reaction time, abnormal balance with the eyes open and with the eyes closed, abnormalities of color confusion index, scotoma in visual fields, reduced verbal recall, digit symbol score, and elevated abnormal moods. The effects on the two groups of 10 were similar and resembled those from formaldehyde exposure but with less cognitive impairment. CONCLUSIONS: Adverse effects from indoor air in manufactured homes and during renovations were less severe but similar to those from occupational formaldehyde exposures. This suggests that formaldehyde has a major role in health problems from indoor air

- (183) Reitzig M, Mohr S, Heinzow B, Knoppel H. VOC Emissions after Building Renovations: Traditional and Less Common Indoor Air Contaminants, Potential Sources, and Reported Health Complaints. *Indoor Air*. 1998;8:91-102.
Abstract: Volatile organic compounds (VOCs) were measured in the air of 51 renovated rooms in Schleswig-Holstein. The buildings examined were of different types - private flats, schools, kindergartens, office buildings - the only common characteristic being that they had all been renovated within the last two years. Among the dominating substances in the 46/51 complaint cases were well-known substances such as alkylbenzenes or monoterpenes at high concentrations but also less common substances, i.e. those which have only recently been reported as indoor air contaminants, for example phenoxyethanol, 2-(2-butoxyethoxy)-ethylacetate (butyldiglycolacetate) or longifolene (Mohr, 1994) at remarkable concentrations. A tentative investigation was made to identify the simultaneous occurrences of the different substances, especially the uncommon ones with their potential sources, as well as health impairments. Finally, VOC emissions from two carpet glues, suspected during the investigations of playing a role as a potential source of the less common substances, were carefully measured under test chamber conditions. This additional laboratory experiment was made to verify the tendency shown in the field study that modern ecological building materials contain less volatile and less common substances but with increased indoor persistence, that could partially account for the increasing number of complaints in relation to the SBS phenomenon
- (184) Canada Green Building Council. Green Building Rating System for New Construction & Major Renovations LEED Canada-NC Version 1.0. Canada Green Building Council . 2004.
http://www.cagbc.org/uploads/FINAL_LEED%20CANADA-NC%201.0_Green%20Building%20Rating%20System.pdf available from
http://www.cagbc.org/building_rating_systems/leed_rating_system.php
Abstract: Through its use as as design guideline and third-party certification tool, LEED aims to improve occupant well-being, environmental performance and economic returns of buildings using established and innovative practices, standards and technologies. It provides one definition, widely accepted by industry, for what currently constitutes a "green building." LEED Canada-NC 1.0 consists of an explicit set of environmental performance criteria, organized within five key performance categories: Sustainable Sites; Water Efficiency; Energy and Atmosphere; Materials and Resources, and Indoor Environmental Quality. A sixth category, Innovation and Design Process, rewards exceptional environmental performance or innovation over and above that explicitly covered in the basic LEED credits.
- (185) Yura A, Iki M, Shimizu T. [Indoor air pollution in newly built or renovated elementary schools and its effects on health in children]. *Nippon Koshu Eisei Zasshi*. 2005;52:715-726.

Abstract: **PURPOSE:** To elucidate the actual status of indoor air pollution at newly built or renovated elementary schools, and to evaluate its effects on health symptoms in the affected children. **METHODS:** In the classrooms of four newly built or renovated elementary schools in Osaka Prefecture, indoor air levels of formaldehyde and volatile organic compounds (VOC) were measured immediately, 1 month, 3 months, 10 months and 22 months after the completion of the construction work. Also, questionnaire surveys regarding subjective symptoms of sick building syndrome were conducted before and after the renovation on the children who attended classes in the renovated rooms. **RESULTS:** In the newly built computer classroom, more formaldehyde was detected one month after the completion of the construction work, when computers and furniture were carried in, than immediately after the completion of the work. Then, during the summer season, even 10 months and 22 months after completion of the new building, formaldehyde above the guideline values was detected. In the renovated common classrooms, the formaldehyde level was the same as that in the classrooms which did not undergo renovation, but VOC levels were higher immediately after the completion of the construction work, and the toluene level was above the guideline value. In 4-story reinforced concrete school buildings, indoor air pollution tended to be higher on the third and the fourth floors than on the first and the second floors. In 3-story school buildings, indoor air pollution tended to be higher on the third floor than on the second floor. The survey of subjective symptoms of the children revealed a tendency toward an increase in the prevalence of sick building syndrome after a renovation. However, the actual number of the children complaining of the symptoms hardly changed. Instead, the number of symptoms for each subject increased, and this increase was significant in 5th and 6th grade boys. **CONCLUSION:** In the some classrooms of newly built or renovated elementary schools, chemical substances above the guideline values may be detected. In such classrooms, more ventilation is required

- (186) Molhave L, Dueholm S, Jensen LK. Assessment of Exposures and Health Risks Related to Formaldehyde Emissions from Furniture: a Case Study. *Indoor Air*. 1995;5:104-119.
- Abstract: Abstract According to the Californian Safe Drinking Water and Toxic Enforcement Act, Proposition 65 (State of California, 1986) the manufacturers and retailers of products (such as furniture and fittings) which emit formaldehyde are obliged to either mark their products with a warning label or provide evidence that their products do not pose a significant cancer risk to the consumer. The significant risk is defined as 1 case of cancer in a population of 100,000 persons within a period of exposure of 70 years (State of California, 1992). In this study, a large-scale climate chamber test of a full set of furniture and fitments was made. The formaldehyde concentration in a test chamber peaked at about 112 mug/m³ within a day after the furniture had been installed. After 8 weeks the concentration leveled out at about 50 mug/m³. Various models were used to predict occupant exposures in homes containing the same furniture and fitments; multi-compartment models identified a short-term compartment with a half-life of between 5.2 and 6.0 h and a relative source strength of between 75% and 30% of the total source strength; a medium-term compartment with a half-life of between 14 and 81 days; and a long-term compartment for which the best estimate of a half-life was 384 days. The accumulated dose of formaldehyde absorbed by an occupant during 70 years of exposure in the hypothetical home was estimated by extrapolation using the same models. The dose was found to be in the range of 0.13 g to 0.16 g. The concentration in the test chamber showing a maximum value of 112 mug/m³ formaldehyde may cause discomfort among hypersensitive persons during the first couple of days. The risk estimates based on the estimated long-term dose indicate that the cancer risks associated with the exposure caused by furniture are in the range of 6.9 to 8.9 x 10⁻⁸, based on monkey data, and 5.8 to 7.4 x 10⁻⁷, based on rat data. In conclusion, a successful draft protocol was established for tests in relation to Proposition 65

and, with the limitations of this exploratory study, the actual furniture equipment is considered to cause no significant cancer risk to the consumer according to the Proposition

- (187) Greenpeace. Guide to Greener Electronics. 18-9-2006.

<http://www.greenpeace.org/raw/content/international/press/reports/greener-electronics-guide.pdf> available from greenpeace.org/electronics

Abstract: Substituting harmful chemicals in the production of electronics will prevent worker exposure to these substances and contamination of communities that neighbour production facilities. Eliminating harmful substances will also prevent leaching/off-gassing of chemicals like brominated flame retardants (BFR) during use, and enable electronic scrap to be safely recycled. The presence of toxic substances in electronics perpetuates the toxic cycle - during reprocessing of electronic waste and by using contaminated secondary materials to make new products. Until the use of toxic substances is eliminated, it is impossible to secure 'safe' recycling. For this reason, the points awarded to corporate practice on chemicals (five criteria, double points for PVC - and BFR-free models) are weighted more heavily than criteria on recycling, because until the use of harmful substances is eliminated in products, it is impossible to secure 'safe', toxic-free recycling.

HP loses point: In September 2006, one penalty point was deducted from HP's overall score when testing of an HP laptop revealed the presence of a type of brominated flame retardant, known as decaBDE. In its Global Citizen Report 2006, HP states: "HP eliminated the use of decaBDE many years ago and has no plans to reinitiate its use." Moreover, of the five brands of laptops tested by Greenpeace with results released in 2006, only the HP laptop was found to contain lead.

- (188) Bridges B. Fragrances and allergic reactions. *J Am Board Fam Pract.* 2001;14:400a-4401.

Abstract: The use of scented products has increased dramatically since the 1970s. Formulations of scented products have also been changed. More than 80 to 90 percent of fragrance materials are now synthesized, the most from petrochemicals. Powerful synthetic materials are used at higher levels, and three to five compounds might make up to 80 percent of the fragrance formula. Products are designed to be strong and tenacious. Fragrances are complex mixtures of volatile compounds, most with little available health and safety data. Fragrances pose many health concerns. They add to indoor air pollution and are respiratory irritants. There are no tests to determine whether they are respiratory allergens, but they are frequently cited by asthmatics as causing or triggering asthma. The Institute of Medicine (IOM), at the request of the Environmental Protection Agency, reviewed the medical literature on the impact of fragrances on asthma. The IOM placed fragrances in the same category as second-hand smoke in triggering and exacerbating asthma in school-age children and adults.² Respiratory effects are not the only concerns related to fragrance. Fragrance is second only to nickel as a skin allergen.³ Phthalates used in fragrances are suspected of being hormone disruptors.⁴ Synthetic musk compounds bioaccumulate in human tissue and are found in breast milk.⁵ Citral, a common fragrance flavor compound, causes enlargement of the prostate gland and has estrogenic effects.⁶ Fragrance is also a frequent trigger for migraines.

- (189) Bridges B. Fragrance: emerging health and environmental concerns. *Flavour Fragr J* 17, 361-371. 2002. 17-1-2007.

Abstract: Products containing scent are a part of daily life. The majority of cosmetics, toiletries, household and laundry products contain fragrance. In addition, there is exposure to fragrance from products that are used to scent the air, such as air fresheners and fragranced candles. In spite of this widespread use and exposure, there is little information available on the materials

used in fragrance. Fragrance formulas are considered trade secrets and components that make up the fragrance portion of the product are not revealed on labels. Fragrance is increasingly cited as a trigger in health conditions such as asthma, allergies and migraine headaches. In addition, some fragrance materials have been found to accumulate in adipose tissue and are present in breast milk. Other materials are suspected of being hormone disruptors. The implications are not fully known, as there has been little evaluation of systemic effects. There are environmental concerns as well, as fragrances are volatile compounds, which add to both indoor and outdoor air pollution. Synthetic musk compounds are persistent in the environment and contaminate waterways and aquatic wildlife. At present there is little governmental regulation of fragrance. The fragrance industry has in place a system of self-regulation. However, the present system has failed to address many of the emerging concerns. Industry needs to responsibly address concerns and ensure that scented products are safe for users, those inadvertently exposed and the environment. It is essential that an industry that is, and wishes to continue to be, self-regulated should identify and address concerns in a forthright and responsible manner.

- (190) Anderson RC, Anderson JH. Acute toxic effects of fragrance products. *Arch Environ Health*. 1998;53:138-146.

Abstract: To evaluate whether fragrance products can produce acute toxic effects in mammals, we allowed groups of male Swiss-Webster mice to breathe the emissions of five commercial colognes or toilet water for 1 h. We used the ASTM-E-981 test method to evaluate sensory irritation and pulmonary irritation. We used a computerized version of this test to measure the duration of the break at the end of inspiration and the duration of the pause at the end of expiration. Decreases in expiratory flow velocity indicated airflow limitation. We subjected the mice to a functional observational battery to probe for changes in nervous system function. The emissions of these fragrance products caused various combinations of sensory irritation, pulmonary irritation, decreases in expiratory airflow velocity, as well as alterations of the functional observational battery indicative of neurotoxicity. Neurotoxicity was more severe after mice were repeatedly exposed to the fragrance products. Evaluation of one of the test atmospheres with gas chromatography/mass spectrometry revealed the presence of chemicals for which irritant and neurotoxic properties had been documented previously. In summary, some fragrance products emitted chemicals that caused a variety of acute toxicities in mice

- (191) Lessenger JE. Occupational acute anaphylactic reaction to assault by perfume spray in the face. *J Am Board Fam Pract*. 2001;14:137-140.

Abstract: Background: Perfumes have been associated with rashes in employees exposed to scented soaps or with allergic conditions, such as rhinitis or asthma, in employees exposed to perfumes or fragrances in the air.

Methods: Reported here is a case of an anaphylactic reaction and respiratory distress as a result of a deliberate assault with a perfume spray. The medical literature was searched using the key words "fragrances," "respiratory distress," "assault," and "health care workers."

Results: A female medical assistant with no history of asthma or reactions to fragrances was assaulted by a patient, who pumped three sprays of a perfume into her face. The employee experienced an acute anaphylactic reaction with shortness of breath, a suffocating sensation, wheezes, and generalized urticaria, and required aggressive medical treatment, a long period of oral bronchodilator therapy, and, finally, weaning from the medications.

Conclusions: Perfumes are complex mixtures of more than 4,000 vegetable and animal extracts and organic and nonorganic compounds. Fragrances have been found to cause exacerbations of symptoms and airway obstruction in asthmatic patients, including chest tightening and

wheezing, and are a common cause of cosmetic allergic contact dermatitis. In many work settings the use of fragrances is limited. Assault is becoming more common among workers in the health care setting. Workers should be prepared to take immediate steps should an employee go into anaphylactic shock.

- (192) Public Service Alliance of Canada. PSAC Awareness kit on scent-free environments (Chemical Sensitivities - Environmental Illness). PSAC . 1998. http://www.psacbc.com/wp-content/uploads/2006/01/scent_free_web_e.pdf

Abstract: Multiple Chemical Sensitivity (MCS) is basically a subset of Environmental Illness (EI), which is caused by living in a toxic world. The chemicals that were synthesized after World War II (including, pesticides, synthetic fragrances, cleaning products, detergents, etc.) are mostly "petro-chemicals" (petroleum based) and are quite toxic to humans. There have been virtually no studies done on the majority of these chemicals to see how they affect humans. The industry just placed the chemicals in the environment with the assumption that they are "safe, till proven toxic", instead of the other way around. One of the biggest offenders is PERFUME and other scented products. Did you know that many of the ingredients in your perfume are the exact same ingredients found in GASOLINE??!! The scary thing is that the perfume industry is NOT REGULATED at all. They can put any number of chemicals in fragrance without revealing what those chemicals are or how they affect humans.

Some toxic chemicals found in fragrances Toluene, ethanol, acetone, formaldehyde, limonene, benzene derivatives, ethylene chloride, and many others known to cause cancer, birth defects, infertility, nervous system damage, or other injuries. The U.S. Environmental Protection Agency (EPA) even found chloroform in fabric softeners.

As Romantic as Hazardous Waste Toluene was found in every fragrance sample collected by the U.S. Environmental Protection Agency for a 1991 report. "Toluene was most abundant in the auto parts store as well as the fragrance section of the department store." Toluene has been proven to cause cancer and nervous system damage and is designated as hazardous waste.

Not Just in a Perfume Bottle There is a dramatic increase in people who are made sick by fragrances because so many products are now scented. Babies and children are even more vulnerable, as are people who are trying to recover from cancer and other illnesses.

Chemical fragrances are present in most laundry detergents, fabric softeners, anti-cling products, dishwashing liquids, disinfectants, soaps, shampoos and other hair products, deodorants, cosmetics, suntan/sunscreen lotions, aftershaves, colognes, incense, analgesic creams, and lip balms. Even products marked "unscented" often are falsely labeled and actually contain toxic fragrances.

Perfume Pollutes Using environmentally safe products is as important as recycling. If everyone stopped buying unsafe, chemically-scented products, companies would stop making them, ending a lot of unnecessary pollution.

Scents and Illness Exposure to scented products can cause exhaustion, weakness, "hay fever" symptoms, dizziness, difficulty concentrating, headaches, rashes, swollen lymph glands, muscle aches and spasms, heart palpitations, nausea, stomach cramps, vomiting, asthma attacks (inability to breathe), neuromotor dysfunction, seizures, and loss of consciousness.

MCS (Multiple Chemical Sensitivities) is caused by overexposure to toxic chemicals. Even if you don't feel the effects yet, your health is still being damaged, and you will develop MCS or other illnesses if you continue to be exposed to toxic chemicals.

Some Safer Products Fabric softeners, anti-cling products, disinfectants, other strongly-scented products, and most detergents have toxic ingredients. If you use hair mousse and gels, hairspray or if you chemically process your hair, it will need many washings with a safe shampoo and the passage of time before you can be around someone with MCS without making them ill. What

may seem like a mild fragrance to you can be excruciatingly toxic to someone with MCS. Some safer products are available in local health-food stores or from mail-order stores. Keep in mind that tolerance to a particular product varies from one individual to another. For your convenience a short list of safer products is attached to this document as Appendix A. The PSAC does not endorse any of the products found on the list but is providing it as an initial informative tool only.

- (193) Small BM. Creating mold-free buildings: a key to avoiding health effects of indoor molds. *Arch Environ Health*. 2003;58:523-527.

Abstract: In view of the high costs of building diagnostics and repair subsequent to water damage--as well as the large medical diagnostic and healthcare costs associated with mold growth in buildings--commitment to a philosophy of proactive preventive maintenance for home, apartment, school, and commercial buildings could result in considerable cost savings and avoidance of major health problems among building occupants. The author identifies common causes of mold growth in buildings and summarizes key building design and construction principles essential for preventing mold contamination indoors. Physicians and healthcare workers must be made aware of conditions within buildings that can give rise to mold growth, and of resulting health problems. Timely advice provided to patients already sensitized by exposure to molds could save these individuals, and their families, from further exposures as a result of inadequate building maintenance or an inappropriate choice of replacement housing

- (194) Lee TG. Health symptoms caused by molds in a courthouse. *Arch Environ Health*. 2003;58:442-446.

Abstract: A majority of occupants of a newly renovated historic courthouse in Calgary, Alberta, Canada, reported multiple (3 or more) health-related symptoms, and several reported more than 10 persistent symptoms. Most required at least 1 day outside of the building to recover from their symptoms. Molds that produce mycotoxins, such as *Stachybotrys chartarum* and *Emericella nidulans*, were identified in the building, along with fungal organisms of the genera *Aspergillus*, *Penicillium*, *Streptomyces*, *Cladosporium*, *Chaetomium*, *Rhizopus/Mucor*, *Alternaria*, *Ulocladium*, and *Basidiomycetes*. Renovations to this historic had building failed to provide adequate thermal and vapor barriers, thus allowing moist indoor air to migrate into the building enclosure, causing condensation to develop. Mold grew on the condensation and was dispersed throughout the courthouse, including on furniture and files. The courthouse was closed and a new facility was modified with low-offgassing materials, better ventilation and air filtration, and strict building maintenance to accommodate those occupants of the older building who had developed multiple chemical sensitivities

- (195) Shoemaker RC, House DE. Sick building syndrome (SBS) and exposure to water-damaged buildings: time series study, clinical trial and mechanisms. *Neurotoxicol Teratol*. 2006;28:573-588.

Abstract: Occupants of water-damaged buildings (WDBs) with evidence of microbial amplification often describe a syndrome involving multiple organ systems, commonly referred to as "sick building syndrome" (SBS), following chronic exposure to the indoor air. Studies have demonstrated that the indoor air of WDBs often contains a complex mixture of fungi, mycotoxins, bacteria, endotoxins, antigens, lipopolysaccharides, and biologically produced volatile compounds. A case-series study with medical assessments at five time points was conducted to characterize the syndrome after a double-blinded, placebo-controlled clinical trial conducted among a group of study participants investigated the efficacy of cholestyramine

(CSM) therapy. The general hypothesis of the time series study was that chronic exposure to the indoor air of WDBs is associated with SBS. Consecutive clinical patients were screened for diagnosis of SBS using criteria of exposure potential, symptoms involving at least five organ systems, and the absence of confounding factors. Twenty-eight cases signed voluntary consent forms for participation in the time-series study and provided samples of microbial contaminants from water-damaged areas in the buildings they occupied. Twenty-six participants with a group-mean duration of illness of 11 months completed examinations at all five study time points. Thirteen of those participants also agreed to complete a double-blinded, placebo-controlled clinical trial. Data from Time Point 1 indicated a group-mean of 23 out of 37 symptoms evaluated; and visual contrast sensitivity (VCS), an indicator of neurological function, was abnormally low in all participants. Measurements of matrix metalloproteinase 9 (MMP9), leptin, alpha melanocyte stimulating hormone (MSH), vascular endothelial growth factor (VEGF), immunoglobulin E (IgE), and pulmonary function were abnormal in 22, 13, 25, 14, 1, and 7 participants, respectively. Following 2 weeks of CSM therapy to enhance toxin elimination rates, measurements at Time Point 2 indicated group-means of 4 symptoms with 65% improvement in VCS at mid-spatial frequency—both statistically significant improvements relative to Time Point 1. Moderate improvements were seen in MMP9, leptin, and VEGF serum levels. The improvements in health status were maintained at Time Point 3 following a 2-week period during which CSM therapy was suspended and the participants avoid re-exposure to the WDBs. Participants reoccupied the respective WDBs for 3 days without CSM therapy, and all participants reported relapse at Time Point 4. The group-mean number of symptoms increased from 4 at Time Point 2 to 15 and VCS at mid-spatial frequency declined by 42%, both statistically significant differences relative to Time Point 2. Statistically significant differences in the group-mean levels of MMP9 and leptin relative to Time Point 2 were also observed. CSM therapy was reinstated for 2 weeks prior to assessments at Time Point 5. Measurements at Time Point 5 indicated group-means of 3 symptoms and a 69% increase in VCS, both results statistically different from those at Time Points 1 and 4. Optically corrected Snellen Distance Equivalent visual acuity scores did not vary significantly over the course of the study. Group-mean levels of MMP9 and leptin showed statistically significant improvement at Time Point 5 relative to Time Points 1 and 4, and the proportion of participants with abnormal VEGF levels was significantly lower at Time Point 5 than at Time Point 1. The number of participants at Time Point 5 with abnormal levels of MMP9, leptin, VEGF, and pulmonary function were 10, 10, 9, and 7, respectively. The level of IgE was not re-measured because of the low incidence of abnormality at Time Point 1, and MSH was not re-measured because previously published data indicated a long time course for MSH improvement. The results from the time series study supported the general study hypothesis that exposure to the indoor air of WDBs is associated with SBS. High levels of MMP9 indicated that exposure to the complex mixture of substances in the indoor air of the WDBs triggered a pro-inflammatory cytokine response. A model describing modes of action along a pathway leading to biotoxin-associated illness is presented to organize current knowledge into testable hypotheses. The model links an inflammatory response with tissue hypoxia, as indicated by abnormal levels of VEGF, and disruption of the proopiomelanocortin pathway in the hypothalamus, as evidenced by abnormalities in leptin and MSH levels. Results from the clinical trial on CSM efficacy indicated highly significant improvement in group-mean number of symptoms and VCS scores relative to baseline in the 7 participants randomly assigned to receive 2 weeks of CSM therapy, but no improvement in the 6 participants assigned placebo therapy during that time interval. However, those 6 participants also showed a highly significant improvement in group-mean number of symptoms and VCS scores relative to baseline following a subsequent 2-week period of CSM therapy. Because the only known benefit of CSM therapy is to enhance the elimination rates of substances that

accumulate in bile by preventing re-absorption during enterohepatic re-circulation, results from the clinical trial also supported the general study hypothesis that SBS is associated with exposure to WDBs because the only relevant function of CSM is to bind and remove toxigenic compounds. Only research that focuses on the signs, symptoms, and biochemical markers of patients with persistent illness following acute and/or chronic exposure to WDBs can further the development of the model describing modes of action in the biotoxin-associated pathway and guide the development of innovative and efficacious therapeutic interventions

- (196) Edmondson DA, Nordness ME, Zacharisen MC, Kurup VP, Fink JN. Allergy and "toxic mold syndrome". *Ann Allergy Asthma Immunol.* 2005;94:234-239.
Abstract: BACKGROUND: "Toxic mold syndrome" is a controversial diagnosis associated with exposure to mold-contaminated environments. Molds are known to induce asthma and allergic rhinitis through IgE-mediated mechanisms, to cause hypersensitivity pneumonitis through other immune mechanisms, and to cause life-threatening primary and secondary infections in immunocompromised patients. Mold metabolites may be irritants and may be involved in "sick building syndrome." Patients with environmental mold exposure have presented with atypical constitutional and systemic symptoms, associating those symptoms with the contaminated environment. OBJECTIVE: To characterize the clinical features and possible etiology of symptoms in patients with chief complaints related to mold exposure. METHODS: Review of patients presenting to an allergy and asthma center with the chief complaint of toxic mold exposure. Symptoms were recorded, and physical examinations, skin prick/puncture tests, and intracutaneous tests were performed. RESULTS: A total of 65 individuals aged 1 1/2 to 52 years were studied. Symptoms included rhinitis (62%), cough (52%), headache (34%), respiratory symptoms (34%), central nervous system symptoms (25%), and fatigue (23%). Physical examination revealed pale nasal mucosa, pharyngeal "cobblestoning," and rhinorrhea. Fifty-three percent (33/62) of the patients had skin reactions to molds. CONCLUSIONS: Mold-exposed patients can present with a variety of IgE- and non-IgE-mediated symptoms. Mycotoxins, irritation by spores, or metabolites may be culprits in non-IgE presentations; environmental assays have not been perfected. Symptoms attributable to the toxic effects of molds and not attributable to IgE or other immune mechanisms need further evaluation as to pathogenesis. Allergic, rather than toxic, responses seemed to be the major cause of symptoms in the studied group
- (197) Vojdani A, Campbell AW, Kashanian A, Vojdani E. Antibodies against molds and mycotoxins following exposure to toxigenic fungi in a water-damaged building. *Arch Environ Health.* 2003;58:324-336.
Abstract: Exposure to molds in water-damaged buildings can cause allergy, asthma, hypersensitivity pneumonitis, mucus membrane irritation, and toxicity--alone or in combination. Despite this, significant emphasis has been placed only on Type I allergy and asthma, but not on the other 3 types of allergies. In this study, we sought to evaluate simultaneous measurements of immunoglobulin (Ig) G, IgM, IgA, and IgE antibodies against the most common molds, and their mycotoxins, cultured from water-damaged buildings. Antibodies against 7 different molds and 2 mycotoxins were determined by enzyme-linked immunosorbent assay (ELISA) in the blood of 40 controls and 40 mold-exposed patients. The IgG antibody levels against all 7 of the molds used, as well as the 2 mycotoxins, were significantly greater in patients than in controls. The IgM antibody levels were significantly different in patients for only 6 of 9 determinations. Regarding IgA determinations, antibodies were elevated significantly against all antigens tested, except *Epicoccum*. However, the differences in IgE levels in controls and mold-exposed patients were significant only for

Aspergillus and satratoxin. These differences implied that, overall, the healthy control group was different from the mold-exposed patients for IgG, IgM, and IgA antibodies, but not for the IgE anti-mold antibody. Most patients with high levels of antibodies against various mold antigens also exhibited elevated antibodies against purified mycotoxins, indicating that the patients had been exposed to mold spores and mycotoxins. Detection of high levels (colony-forming units per cubic meter) of molds--which, in this study, strongly suggested that there existed a reservoir of spores in the building at the time of sampling--along with a significant elevation in IgG, IgM, or IgA antibodies against molds and mycotoxins, could be used in future epidemiologic investigations of fungal exposure. In addition to IgE, measurements of IgG, IgM, and IgA antibodies should be considered in mold-exposed individuals

- (198) Meyer HW, Wurtz H, Suadican P, Valbjorn O, Sigsgaard T, Gyntelberg F. Molds in floor dust and building-related symptoms in adolescent school children. *Indoor Air*. 2004;14:65-72. Abstract: This stratified cross-sectional epidemiological study included 1053 school children aged 13-17 years. All pupils filled in a questionnaire on building-related symptoms and other relevant health aspects. The following exposure measurements were carried out: room temperature, CO2 level, and relative humidity; building characteristics including mold infestation were assessed, and dust was collected from floors, air, and ventilation ducts during a working day. Dust was examined for endotoxin level, and cultivated for viable molds. We did not find a positive association between building-related symptoms and extent of moisture and mold growth in the school buildings. Five of eight building-related symptoms were significantly and positively associated with the concentration of colony forming units of molds in floor dust: eye irritation, throat irritation, headache, concentration problems, and dizziness. After adjusting for different potentially confounding factors in separate analyses of each symptom, the above-mentioned associations between molds in dust and symptoms were still present, except for concentration problems. However, in none of the analyses was mold exposure the strongest covariate, being secondary to either asthma, hay fever, recent airway infection, or psychosocial factors
- (199) Meyer HW, Wurtz H, Suadican P, Valbjorn O, Sigsgaard T, Gyntelberg F. Molds in floor dust and building-related symptoms among adolescent school children: a problem for boys only? *Indoor Air*. 2005;15 Suppl 10:17-24.:17-24. Abstract: In this stratified cross-sectional study in eight 'wet' and seven 'dry' schools, 1024 adolescent school children reported potentially building-related symptoms (BRS) in self-administrated questionnaires. From their classrooms dust samples were collected from floors, ventilation ducts, and air; settled dust was collected in cardboard boxes over a period of 5 months. Measurements of temperature, relative humidity and CO2 were performed. BRS were strongly associated with personal factors like recent airway infections, hay fever, asthma and psycho-social work load, but also to molds in floor dust and presence of mechanical ventilation. The association between molds in floor dust and BRS has in stratified analyses shown a strong association among adolescent school boys, and no association among adolescent school girls using multivariable analyses controlling for relevant confounders. In contrast to the menstruating school girls, the symptoms among the small group of not yet menstruating girls were associated with the levels of molds in floor dust. Their symptom prevalences were very similar to those of the boys. This finding makes us suggest a new hypothesis: The higher endogenous estrogen levels of sexually matured adolescent females seems to protect them from the effects of molds in dust, despite their overall higher symptom prevalence. PRACTICAL IMPLICATIONS: In this cross-sectional epidemiological study of adolescent school children we found independent significant positive associations between building-related symptoms and

viable molds in floor dust in boys and non-menstruating girls. In contrast, no such associations were seen among menstruating girls. The identification of these two susceptible groups adds further support the relevance of minimizing sources of dust and mold exposure

- (200) Meklin T, Husman T, Vepsalainen A et al. Indoor air microbes and respiratory symptoms of children in moisture damaged and reference schools. *Indoor Air*. 2002;12:175-183.
Abstract: Abstract Microbial indoor air quality and respiratory symptoms of children were studied in 24 schools with visible moisture and mold problems, and in eight non-damaged schools. School buildings of concrete/brick and wooden construction were included. The indoor environment investigations included technical building inspections for visible moisture signs and microbial sampling using six-stage impactor for viable airborne microbes. Children's health information was collected by questionnaires. The effect of moisture damage on concentrations of fungi was clearly seen in buildings of concrete/brick construction, but not in wooden school buildings. Occurrence of *Cladosporium*, *Aspergillus versicolor*, *Stachybotrys*, and actinobacteria showed some indicator value for moisture damage. Presence of moisture damage in school buildings was a significant risk factor for respiratory symptoms in schoolchildren. Association between moisture damage and respiratory symptoms of children was significant for buildings of concrete/brick construction but not for wooden school buildings. The highest symptom prevalence was found during spring seasons, after a long exposure period in damaged schools. The results emphasize the importance of the building frame as a determinant of exposure and symptoms. Practical Implications Moisture damage in schools increased the respiratory symptoms of primary and secondary schoolchildren, but the effect was more clear in the school buildings with concrete/brick frame than in wooden schools. The symptoms accumulated towards the spring term, after prolonged exposure time, which may be an optimal time for doing symptom questionnaire studies. In concrete/brick buildings, the effect of moisture damage was seen as elevated concentrations of airborne fungi. Wooden buildings had higher baseline concentrations but no differences between moisture damaged and reference buildings. In practical case investigations and epidemiological studies, possible reference buildings should be matched for the frame material
- (201) Straus DC, Cooley JD, Wong WC, Jumper CA. Studies on the role of fungi in Sick Building Syndrome. *Arch Environ Health*. 2003;58:475-478.
Abstract: Sick Building Syndrome is a term used to describe symptoms in humans which result from problems with indoor air quality. Common complaints include dyspnea, flu-like symptoms, watering eyes, and allergic rhinitis. Although there is likely no single cause for Sick Building Syndrome, fungal contamination in buildings has increasingly been associated with this spectrum of symptoms. The authors describe 2 case studies, and other experimentation, that have investigated the role of fungi in the occurrence of Sick Building Syndrome
- (202) Ahman M, Lundin A, Musabasic V, Soderman E. Improved Health After Intervention in a School with Moisture Problems. *Indoor Air*. 2000;10:57-62.
Abstract: In a school with floor moisture problems, the personnel had complaints consistent with the sick-building syndrome (SBS). Interventive measures including the laying of a ventilated floor were undertaken to eliminate the emissions. To examine if the intervention resulted in positive health effects, 34 personnel and 336 pupils were interviewed just before the intervention and also 7 months after. Also were interviewed 21 personnel and 224 pupils at an adjacent school serving as a control. Compared with the control school, the problem school showed more complaints, more general symptoms and more symptoms from the eyes, airways and skin, both among the personnel and the pupils. In the post-intervention examinations, the

excess of symptoms among the personnel had almost disappeared. Among the pupils, the frequency of eye irritation was reduced but a general improvement of the other symptoms was not as obvious. However, after adjustment for a recent common cold, atopy and stress among the pupils, only one symptom ("stuffy nose") remained significantly elevated. In conclusion, the intervention was followed by positive health effects, supporting the hypothesis that emissions from building material had contributed to the excess of symptoms. A recent common cold was highly related to the symptoms and should be considered in future SBS studies

- (203) Ebbehøj NE, Hansen MO, Sigsgaard T, Larsen L. Building-related symptoms and molds: a two-step intervention study. *Indoor Air*. 2002;12:273-277.
Abstract: AIMS: To evaluate the relation between mold growth and symptoms in an intervention study design. METHODS: The building was examined by a walk-through and microbiological testing from surfaces and ventilation canals before and after each of two steps of the renovation. The examination program for the 25 employees comprised questionnaire, clinical examination, 2-week peak-flow monitoring, and blood samples, and in six persons also a bronchial challenge. RESULTS: Initially the building had severe moisture problems with growth of *Trichoderma* and *Phoma* as dominating microfungi. The total number of symptoms from a nine-item building-related symptom score was 66%, peak-flow variability was 20%. After the first renovation, no visible mold growth was seen, but samples showed that the building was still contaminated. Symptoms decreased to 33%. After further cleaning the mold levels decreased on surfaces, and the number of symptoms decreased to 4%. Mean peak-flow variability fell to 15%. DISCUSSION: In a poorly maintained building with moisture problems and mold growth, the staff had a number of irritative and general symptoms. The first renovation eradicated most visible signs of molds and gave a decreased number of symptoms. The second renovation sufficiently cleaned the building, and the rate of symptoms and peak-flow variability fell to normal levels. A thorough cleaning after renovation seems necessary for the eradication of symptoms
- (204) Centers for Disease Control. U.S. Department of Health and Human Services. Respiratory Infection - Pennsylvania. *Morbidity and Mortality Weekly Report*. 1997;46:49-56.
Abstract: Reprinted below is the initial report published August 6, 1976, on an outbreak of respiratory illness among persons who attended an American Legion convention in Philadelphia during the summer of 1976. Following that report is the special issue of MMWR published January 18, 1977, which announced the identification of the bacterium that caused Legionnaires disease.
- (205) Hirvonen M-R, Huttunen K, Roponen M. Bacterial strains from moldy buildings are highly potent inducers of inflammatory and cytotoxic effects. *Indoor Air*. 2005;15:65-70.
Abstract: Abstract We aimed to identify inflammatory and cytotoxic potential of individual indoor air bacterial and fungal strains, as well as extracts of indoor air filter samples containing bacteria and fungi. Mouse RAW264.7 macrophages were exposed in vitro to four bacterial strains; *Streptomyces californicus*, *Mycobacterium terrae*, *Bacillus cereus* and *Pseudomonas fluorescens*, and three fungal strains; *Penicillium spinulosum*, *Aspergillus versicolor* and *Stachybotrys chartarum*. Furthermore, RAW264.7 macrophages were exposed to indoor air filter sample extracts representing 'low' (n = 21) and 'high' (n = 20) exposure to viable fungi or bacteria. Production of nitric oxide (NO), tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) as well as cell viability were measured after 24 h exposure. The results show that the bacterial strains induce more profound production of NO, TNF-alpha and IL-6 than the studied fungal strains. They also decrease the viability of mouse macrophages.

Similarly, the indoor air filter samples with high concentration of bacteria induced a statistically significant increase in TNF-alpha and IL-6 production as well as a decrease in cell viability. Altogether, these results suggest that indoor air bacterial strains are potent inducers of inflammatory responses and thus possibly related to adverse health effects of the inhabitants. Practical Implications There is abundant documentation of the association between building dampness and mold and adverse health effects on occupants, but the causal agents of the effects are still unclear. In order to reveal these causal links, experimental studies with in vitro and in vivo methods are needed. The present findings shed new light on studies of the microbial constituents of indoor air in moldy buildings responsible for adverse health effects. These results imply that bacteria should also be monitored in cases of suspected microbial contamination of indoor air

- (206) Warsco K, Lindsey PF. Proactive approaches for mold-free interior environments. *Arch Environ Health*. 2003;58:512-522.

Abstract: Interior design education and practice can contribute to the prevention of mold growth in indoor environments. The authors provide an overview of current thinking within the interior design educational and professional communities regarding proactive approaches to achieving mold-free building interiors, including identification of current best practices for the prevention of mold problems in buildings. They also discuss the development of certification programs. A review of recent literature points to the need for interior designers to be educated to specify the use of ecologically sound materials that support the health of building occupants. The authors present trade-offs between best practices for designing mold-free indoor environments (including considerations of cost, maintenance, and operation) and occupant comfort, health, and well-being

- (207) Brandt M, Brown C, Burkhart J, Burton N, Cox-Ganser J, Damon S, Falk H, Fridkin S, Garbe P, McGeehin M, Morgan J, Page E, Rao C, Redd S, Sinks T, Trout D, Wallingford K, Warnock D, and Weissman D. Mold Prevention Strategies and Possible Health Effects in the Aftermath of Hurricanes and Major Floods. *Morbidity and Mortality Weekly Report* 55[RR08], 1-27. 2006. Centers for Disease Control. USA. available from

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5508a1.htm>

Abstract: Extensive water damage after major hurricanes and floods increases the likelihood of mold contamination in buildings. This report provides information on how to limit exposure to mold and how to identify and prevent mold-related health effects. Where uncertainties in scientific knowledge exist, practical applications designed to be protective of a person's health are presented. Evidence is included about assessing exposure, clean-up and prevention, personal protective equipment, health effects, and public health strategies and recommendations. The recommendations assume that, in the aftermath of major hurricanes or floods, buildings wet for >48 hours will generally support visible and extensive mold growth and should be remediated, and excessive exposure to mold-contaminated materials can cause adverse health effects in susceptible persons regardless of the type of mold or the extent of contamination.

For the majority of persons, undisturbed mold is not a substantial health hazard. Mold is a greater hazard for persons with conditions such as impaired host defenses or mold allergies. To prevent exposure that could result in adverse health effects from disturbed mold, persons should 1) avoid areas where mold contamination is obvious; 2) use environmental controls; 3) use personal protective equipment; and 4) keep hands, skin, and clothing clean and free from mold-contaminated dust.

Clinical evaluation of suspected mold-related illness should follow conventional clinical guidelines. In addition, in the aftermath of extensive flooding, health-care providers should be

watchful for unusual mold-related diseases. The development of a public health surveillance strategy among persons repopulating areas after extensive flooding is recommended to assess potential health effects and the effectiveness of prevention efforts. Such a surveillance program will help CDC and state and local public health officials refine the guidelines for exposure avoidance, personal protection, and clean-up and assist health departments to identify unrecognized hazards.

- (208) Shusterman D, Balmes J, Avila PC, Murphy MA, Matovinovic E. Chlorine inhalation produces nasal congestion in allergic rhinitics without mast cell degranulation. *Eur Respir J*. 2003;21:652-657.
Abstract: Seasonal allergic rhinitic (SAR) subjects are more sensitive to nasal irritants than nonrhinitic (NR) subjects; however, the mechanism underlying this difference is unclear. This study sought to determine whether irritant-induced nasal congestion involves mast cell degranulation. Eight SAR and eight NR subjects were exposed to both 1.0 parts per million chlorine and filtered air in separate visits; exposures were via nasal mask and lasted 15 min. Rhinomanometry was performed before, immediately after and 15 min after exposure. Following > or = 2 weeks, exposures and symptom reporting were repeated with nasal lavage, rather than rhinomanometry, pre- and postexposure. A separate substudy using rye grass antigen provided a positive control. Mast cell tryptase was measured in nasal lavage fluid from both substudies using an automated fluoroenzyme immunoassay. Chlorine provocation significantly increased nasal airway resistance in SAR but not NR subjects. Conversely, tryptase levels in nasal lavage fluid were unaffected. Nasal allergen challenge significantly increased both nasal obstruction and nasal lavage tryptase in SAR subjects. Irritant-induced nasal congestion is more pronounced among seasonal allergic rhinitic than nonrhinitic subjects. However, unlike nasal allergen challenge, the mechanism of response to chlorine does not appear to involve mast cell degranulation
- (209) Gorguner M, Aslan S, Inandi T, Cakir Z. Reactive airways dysfunction syndrome in housewives due to a bleach-hydrochloric acid mixture. *Inhal Toxicol*. 2004;16:87-91.
Abstract: The sudden onset of asthmalike symptoms and persistence of airway reactivity following an acute exposure to an irritant gas or vapor has been termed reactive airways dysfunction syndrome (RADS). A mixture of sodium hypochlorite (bleach, 40%) and hydrochloric acid (18%) is commonly used as a household cleaning solution in our region. From this mixture, chlorine gas is produced, which can cause airway damage and ensuing RADS. Here we describe findings of patients with RADS due to this cleaning mixture, and determine factors associated with a favorable outcome. Data were collected retrospectively on 55 symptomatic patients presenting to our emergency department after inhalation exposure to a mixture of bleach and hydrochloric acid. Symptoms, past medical and smoking history, details of the exposure, initial peak expiratory flow rate (PEFR) and oxygenation, and acute reversibility of airways obstruction were documented. All patients met previously defined criteria for the diagnosis of RADS, but did not undergo methacholine challenge testing and bronchoalveolar lavage or histopathologic study. Fifty patients were followed over the course of 3 mo. The majority of exposures (64%) occurred in the bathroom or kitchen. Only 21 of 55 (38%) patients showed an improvement in PEFR of 15% or greater following two beta(2)-agonist inhalation treatments. In follow-up, 48 patients (87%) improved clinically and functionally (FEV(1)). Seven patients (13%) deteriorated, with ARDS developing in two, one of whom died from respiratory failure. Advanced age, initial low PEFR, exposure in a small enclosed area, use immediately after mixing, and prolonged short- and long-term exposures were associated with a poorer prognosis. This descriptive study is the largest case series in the

literature of RADS developing after exposure to a bleach-hydrochloric acid mixture. The optimum acute treatment and long-term outcomes for patients with RADS due to this combination still need to be determined

- (210) Shusterman D, Murphy MA, Walsh P, Balmes JR. Cholinergic blockade does not alter the nasal congestive response to irritant provocation. *Rhinology*. 2002;40:141-146.
Abstract: OBJECTIVE: To understand the mechanism underlying the nasal congestive response to irritant challenge. METHODS: We exposed 22 subjects--8 with seasonal allergic rhinitis (SAR), 6 with perennial allergic rhinitis (PAR), and 8 normals--to chlorine (Cl₂) gas (1.0 ppm x 15 min.) by nasal CPAP mask. Control exposures (filtered air) were carried out on separate days, with counter-balancing of exposure order. Nasal airway resistance (NAR) was measured in triplicate before and after the provocation sequence using active posterior rhinomanometry. For each subject, this experiment was repeated twice, after [double-blinded] pre-treatment with: 1) ipratropium bromide (IB) 0.6% nasal spray, and 2) vehicle. RESULTS: As a group, allergic rhinitics (SAR + PAR) showed greater [Cl₂] exposure-related increases in NAR than did normals on placebo (vehicle) pretreatment days ($p < 0.05$). IB pre-treatment, however, did not have a systematic effect on Cl₂-induced congestion. CONCLUSION: Cholinergic mechanisms do not appear to be responsible for the nasal congestive response to irritant provocation
- (211) Thickett KM, McCoach JS, Gerber JM, Sadhra S, Burge PS. Occupational asthma caused by chloramines in indoor swimming-pool air. *Eur Respir J*. 2002;19:827-832.
Abstract: The first series of three workers who developed occupational asthma following exposure to airborne chloramines in indoor chlorinated swimming pools is reported. Health problems of swimmers in indoor pools have traditionally been attributed to the chlorine in the water. Chlorine reacts with bodily proteins to form chloramines; the most volatile and prevalent in the air above swimming pools is nitrogen trichloride. Two lifeguards and one swimming teacher with symptoms suggestive of occupational asthma kept 2-hourly measurements of peak expiratory flow at home and at work, analysed using the occupational asthma system (OASYS) plotter, and/or had specific bronchial challenge testing to nitrogen trichloride, or a workplace challenge. Air measurement in one of the pools showed the nitrogen trichloride levels to be 0.1-0.57 mg x m⁻³, which was similar to other studies. Two workers had peak expiratory flow measurements showing occupational asthma (OASYS-2 scores 2.88 and 3.8), both had a positive specific challenge to nitrogen trichloride at 0.5 mg x m⁻³ with negative challenges to chlorine released from sodium hypochlorite. The third worker had a positive workplace challenge. Swimming-pool asthma due to airborne nitrogen trichloride can occur in workers who do not enter the water because of this chloramine. The air above indoor swimming pools therefore needs to be assessed and managed as carefully as the water
- (212) Medina-Ramon M, Zock JP, Kogevinas M et al. Asthma, chronic bronchitis, and exposure to irritant agents in occupational domestic cleaning: a nested case-control study. *Occup Environ Med*. 2005;62:598-606.
Abstract: BACKGROUND: Women employed in domestic cleaning are at increased risk for symptoms of obstructive lung disease, but the agents responsible are unknown. AIMS: To investigate common tasks and products in occupational domestic cleaning in relation to respiratory morbidity. METHODS: Case-control study in domestic cleaning women nested within a large population based survey of women aged 30-65 years; 160 domestic cleaning women with asthma symptoms, chronic bronchitis symptoms, or both and 386 without a history of respiratory symptoms were identified. Detailed exposures were evaluated for 40 cases who reported still having symptoms at the recruitment interview, and 155 controls who reported not

having symptoms. All tasks performed and products used when cleaning houses were determined in a face-to-face interview. Lung function, methacholine challenge, and serum IgE testing were performed. Personal exposure measurements of airborne chlorine and ammonia were performed in a subsample. Associations between asthma, chronic bronchitis, and cleaning exposures were evaluated using multiple logistic regression analysis. RESULTS: Airborne chlorine (median level 0-0.4 ppm) and ammonia (0.6-6.4 ppm) were detectable during occupational domestic cleaning activities. Cases used bleach more frequently than controls; adjusted odds ratio (OR) for intermediate exposure was 3.3 (95% CI 0.9 to 11) and for high exposure 4.9 (1.5 to 15). Other independent associations included accidental inhalation of vapours and gases from cleaning agents and washing dishes. These associations were more pronounced for cases with asthma symptoms than for those with symptoms of chronic bronchitis, but were not related to sensitisation to common allergens. CONCLUSIONS: Asthma symptoms in domestic cleaning women are associated with exposure to bleach and possibly other irritant agents. The public health impact of the use of irritant cleaning products could be widespread since the use of these products is common both in the workplace and at home

- (213) U.S.Environmental Protection Agency Office of Air and Radiation Indoor Environments Division. Mold Remediation in Schools and Commercial Buildings. US EPA . 2007. www.epa.gov/iaq/molds/graphics/moldremediation.pdf
Abstract: This document presents guidelines for the remediation/cleanup of mold and moisture problems in schools and commercial buildings; these guidelines include measures designed to protect the health of building occupants and remediators. It has been designed primarily for building managers, custodians, and others who are responsible for commercial building and school maintenance. It should serve as a reference for potential mold and moisture remediators. Using this document, individuals with little or no experience with mold remediation should be able to make a reasonable judgment as to whether the situation can be handled in-house. It will help those in charge of maintenance to evaluate an in-house remediation plan or a remediation plan submitted by an outside contractor. Contractors and other professionals who respond to mold and moisture situations in commercial buildings and schools may also want to refer to these guidelines.
- (214) Common Ground Collective. EM used to clean up mold. Common Ground Relief . 11-11-2006. <http://www.commongroundrelief.org/em> available from <http://www.commongroundrelief.org>
Abstract: Massive amounts of chlorine bleach are routinely used to deal with the dangerously unsanitary conditions after the hurricanes.
Through generous contributions, Common Ground uses Efficient Microbes (EM) to effectively remove mold from homes, keep fly populations down and promote healthy soil. EM uses probiotics to create "healthy" surfaces. Beneficial microorganisms break down mold and other contaminants, and leave no hazardous chemicals behind.
Using pump sprayers, one gallon of EM can treat 10,000 square feet of space making it very efficient for use in the cleanup in New Orleans.
- (215) Seppanen OA, Fisk WJ. Summary of human responses to ventilation. *Indoor Air*. 2004;14:102-118.
Abstract: Abstract It is known that ventilation is necessary to remove indoor-generated pollutants from indoor air or dilute their concentration to acceptable levels. But as the limit values of all pollutants are not known the exact determination of required ventilation rates based on pollutant concentrations is seldom possible. The selection of ventilation rates has to be based also on epidemiological research, laboratory and field experiments and experience. The existing

literature indicates that ventilation has a significant impact on several important human outcomes including: (1) communicable respiratory illnesses; (2) sick building syndrome symptoms; (3) task performance and productivity, and (4) perceived air quality (PAQ) among occupants or sensory panels (5) respiratory allergies and asthma. In many studies, prevalence of sick building syndrome symptoms has also been associated with characteristics of HVAC-systems. Often the prevalence of SBS symptoms is higher in air-conditioned buildings than in naturally ventilated buildings. The evidence suggests that better hygiene, commissioning, operation and maintenance of air handling systems may be particularly important for reducing the negative effects of HVAC systems. Ventilation may also have harmful effects on indoor air quality and climate if not properly designed, installed, maintained and operated. Ventilation may bring indoors harmful substances or deteriorate indoor environment. Ventilation interacts also with the building envelope and may deteriorate the structures of the building. Ventilation changes the pressure differences across the structures of building and may cause or prevent infiltration of pollutants from structures or adjacent spaces. Ventilation is also in many cases used to control the thermal environment or humidity in buildings. The paper summarises the current knowledge on positive and negative effects of ventilation on health and other human responses. The focus is on office-type working environment and residential buildings. Practical implications The review shows that ventilation has various positive impacts on health and productivity of building occupants. Ventilation reduces the prevalence of airborne infectious diseases and thus the number of sick leave days. In office environment a ventilation rate up to 20-25L/s per person seem to decrease the prevalence of SBS-symptoms. Air conditioning systems may increase the prevalence of SBS-symptoms relative to natural ventilation if not clean. In residential buildings the air change rate in cold climates should not be below app. 0.5ach. Ventilation systems may cause pressure differences over the building envelope and bring harmful pollutants indoors

- (216) Sherman M. ASHRAE's New Residential Ventilation Standard. ASHRAE Journal, January 2004. 2004.
http://utwired.engr.utexas.edu/siegel/ARE381E_S06/references/ASHRAE62_2_sherman.pdf
Abstract: ASHRAE has long been in the business of ventilation, but most of the focus of that effort has been in the area of commercial and institutional buildings. Residential ventilation was traditionally not a major concern because it was believed that, between operable windows and envelope leakage, people were getting enough outside air in their homes. In the three decades since the first oil crisis, houses have become much more energy efficient. At the same time, the kinds of materials and functions in houses changed in character in response to people's needs. People became more environmentally conscious and aware not only about the resources they were consuming but about the environment in which they lived. Homeowners and occupants will benefit from the application of Standard 62.2 and use of the top 10 list.
- (217) Bourbeau J, Brisson C, Allaire S. Prevalence of the sick building syndrome symptoms in office workers before and after being exposed to a building with an improved ventilation system. *Occup Environ Med.* 1996;53:204-210.
Abstract: OBJECTIVE: To find if the prevalence of symptoms associated with sick building syndrome decreased among office workers after moving to a building with improved ventilation (after controlling for potential confounders). METHODS: Workers in five buildings in 1991 all moved in 1992 into a single building with improved design, operation, and maintenance of the ventilation system. All buildings had sealed windows with mechanical ventilation, air conditioning, and humidification. Workers completed a self administered questionnaire during normal working hours in February 1991 and February 1992. The questionnaire encompassed

symptoms of the eyes, nose and throat, respiratory system, skin, fatigue, headache, and difficulty concentrating, personal, psychosocial, and work related factors. During normal office hours of the same week environmental variables were measured. RESULTS: The study population comprised 1390 workers in 1991 and 1371 workers in 1992 who represented more than 80% of the eligible population. The prevalence of most symptoms decreased when workers moved to the new building: skin (54%), respiratory system (53%), nose and throat (46%), fatigue (44%), headache (37%), eyes (23%). These findings were all significant and remained generally similar after controlling for personal, psychosocial, and work related factors. Furthermore, more than 60% of workers symptomatic in 1991 were asymptomatic in 1992 for all types of symptoms. In contrast, less than 15% of workers were asymptomatic in 1991 but symptomatic in 1992 for all types of symptoms. CONCLUSION: In this study, the prevalence of most symptoms usually associated with the sick building syndrome decreased by 40% to 50% after workers were transferred to a building with an improved ventilation system. The results show that it is possible to diminish the prevalence of symptoms associated with the sick building syndrome among office workers occupying a building with mechanical ventilation, air conditioning, and sealed windows

- (218) Wargocki P, Lagercrantz L, Witterseh T, Sundell J, Wyon DP, Fanger PO. Subjective perceptions, symptom intensity and performance: a comparison of two independent studies, both changing similarly the pollution load in an office. *Indoor Air*. 2002;12:74-80.
Abstract: The present paper shows that introducing or removing the same pollution source in an office in two independent investigations, one in Denmark and one in Sweden, using similar experimental methodology, resulted in similar and repeatable effects on subjective assessments of perceived air quality, intensity of sick building syndrome symptoms and performance of office work. Removing the pollution source improved the perceived air quality, decreased the perceived dryness of air and the severity of headaches, and increased typing performance. These effects were observed separately in each experiment and were all significant ($P < \text{or} = 0.05$) after combining the data from both studies, indicating the advantages of pollution source strength control for health, comfort, and productivity
- (219) Abraham ME. Microanalysis of Indoor Aerosols and the Impact of a Compact High-Efficiency Particulate Air (HEPA) Filter System. *Indoor Air*. 1999;9:33-40.
Abstract: Aerosol particles in municipal atmospheres are of increasing public health concern; however, since most of our time is spent indoors, indoor aerosols must be researched in counterpart. Compact High-Efficiency Particulate Air (HEPA) filter systems are commonly employed in residences to alleviate airborne dust concentrations. In this study, a detailed and original methodology was used to determine concentrations and types of submicrometer aerosols, as well as of large ($>4 \mu\text{m}$) dust particles. Scanning electron microscopy was used to quantify and characterize ambient aerosols collected from filtered and non-filtered rooms. Particle concentrations were significantly lower in samples collected in the presence of the filter system (mean 23 to 8 coarse particles liter⁻¹, 63% reduction; 13 to 3 inorganic submicron particles cm⁻³, 76% reduction; 85 to 33 total submicron particles cm⁻³, 62% reduction; all $P < 0.05$). This study provides a new methodology for analysis of indoor aerosols and new data on their physico-chemical characteristics. Since the filter systems are effective at reducing submicron aerosol concentrations, they may improve the health of individuals such as asthmatics, who experience health problems caused by anthropogenic fine particles
- (220) Moritz M, Peters H, Nipko B, Ruden H. Capability of air filters to retain airborne bacteria and molds in heating, ventilating and air-conditioning (HVAC) systems. *Int J Hyg Environ Health*.

2001;203:401-409.

Abstract: The capability of air filters (filterclass: F6, F7) to retain airborne outdoor microorganisms was examined in field experiments in two heating, ventilating and air conditioning (HVAC) systems. At the beginning of the 15-month investigation period, the first filter stages of both HVAC systems were equipped with new unused air filters. The number of airborne bacteria and molds before and behind the filters were determined simultaneously in 14 days-intervals using 6-stage Andersen cascade impactors. Under relatively dry (< 80% R. H.) and warm (> 12 degrees C) outdoor air conditions air filters led to a marked reduction of airborne microorganism concentrations (bacteria by approximately 70% and molds by > 80%). However, during long periods of high relative humidity (> 80% R. H.) a proliferation of bacteria on air filters with subsequent release into the filtered air occurred. These microorganisms were mainly smaller than 1.1 microns therefore being part of the respirable fraction. The results showed furthermore that one possibility to avoid microbial proliferation is to limit the relative humidity in the area of the air filters to 80% R. H. (mean of 3 days), e.g. by using preheaters in front of air filters in HVAC-systems

- (221) Clausen G. Ventilation filters and indoor air quality: a review of research from the International Centre for Indoor Environment and Energy. *Indoor Air*. 2004;14:202-207.
Abstract: Abstract The presence of a used filter in a ventilation system can have an adverse impact on perceived air quality, SBS symptoms, and performance of office work. The present paper reviews the studies leading to this conclusion and discusses recent work that has been performed in a search for the mechanisms involved. One promising hypothesis involves chemical reactions on the surface of the collected particles in the formation of noxious compounds. Finally, a discussion on engineering solutions is presented. Practical implications Loaded particle filters provide a significant source of air pollution. To counteract this, filters should be changed frequently or an alternative method of removing particles from the air should be applied
- (222) Tarkowski M, Lutz W, Birindelli S. The lymphocytic cholinergic system and its modulation by organophosphorus pesticides. *Int J Occup Med Environ Health*. 2004;17:325-337.
Abstract: Clinical and basic mechanism observations reveal interactions between neural and immune systems. These two systems create a complex network for recognizing danger to the host and its protection from outside pathogenic elements as well as from inside overreactions of inflammatory character. Here, we review the interactions of these two systems in relation to the effects of pesticides that clearly involve elements of cholinergic lymphocytic system. We discuss cellular and soluble elements of the immune system, which may be affected by pesticide exposure. We suggest that in-depth studies of the influence of pesticides on lymphocytes may contribute to the development of sensitive methods of measuring early adverse effects appearing in response to pesticide exposure
- (223) Sandborn M, Cole D, Kerr K, Vakil C, Sanin LH, and Bassil K. Ontario College of Family Physicians. Pesticides Literature Review. 2003. 27-8-2006. available from <http://www.ocfp.on.ca/english/ocfp/communications/publications/default.asp?s=1#EnvironmentHealth>
- (224) National Institute of Environmental Health Sciences. Questions and Answers - EMF in the Workplace. <http://www.niehs.nih.gov/emfrapid/html/Q&A-Workplace.html> . 1996.
Abstract: It is a modern fact of life that whether we are at work, at home, or at school, we are all exposed to EMFs-electric and magnetic fields produced by the generation, transmission, and

use of electricity.

Some human health studies suggest that there may be a link between exposure to EMFs and certain types of cancer, primarily leukemia and brain cancer. Some scientists doubt that this apparent connection between EMF exposure and cancer is real, because it is difficult to explain biologically and because the research results are inconsistent. Most agree that more information is needed to resolve the issue about whether or not EMFs affect human health. The U.S. government has initiated a national EMF research effort and important study results are expected in the next few years.

The purpose of this booklet is to provide information about EMF exposure in the workplace. The booklet describes what researchers have learned (and have yet to learn) about EMFs and identifies some sources of EMFs in various industries.

- (225) Havas M. Biological effects of non-ionizing electromagnetic energy: A critical review of the reports by the US National Research Council and the US National Institute of Environmental Health Sciences as they relate to the broad realm of EMF bioeffects. *Environ Rev.* 2000;8:173-253.

Abstract: Our dependence on electricity and our growing dependence on wireless telecommunication technology is causing this planet to be inundated with electromagnetic energy ranging in frequency from less than 60 Hz to greater than 2 GHz. Concerns expressed by the public, who live near power lines, cell phone antennas, or television and radio broadcast towers, have prompted two major reviews: one by the US National Research Council (NRC) and the other by the US National Institute of Environmental Health Science (NIEHS). Both of these documents deal with the biological and health effects primarily in a residential setting of extremely low frequency (ELF) or power frequency (50 and 60 Hz) fields. This paper critically evaluates the NRC and NIEHS documents. This evaluation includes both the content and the process leading to the final reports. It summarizes the information available on human exposure to electric and magnetic fields and identifies key biological markers and potential mechanisms that have been linked to electromagnetic exposure. It examines the conclusions of both documents in terms of the slightly broader realm associated with occupational exposure, non-power frequency fields, EMF hypersensitivity, and response of species other than humans. It presents some of the scientific controversy surrounding the question "Are low frequency electric and magnetic fields harmful?" and examines the concepts of bias and consistency in data interpretation. This paper also attempts to place the discussions about technologically generated fields (technofields) into a much broader perspective, a perspective that includes naturally occurring geofields and biofields.

- (226) Kheifets L, Repacholi M, Saunders R, van DE. The sensitivity of children to electromagnetic fields. *Pediatrics.* 2005;116:e303-e313.

Abstract: In today's world, technologic developments bring social and economic benefits to large sections of society; however, the health consequences of these developments can be difficult to predict and manage. With rapid advances in electromagnetic field (EMF) technologies and communications, children are increasingly exposed to EMFs at earlier and earlier ages. Consistent epidemiologic evidence of an association between childhood leukemia and exposure to extremely low frequency (ELF) magnetic fields has led to their classification by the International Agency for Research on Cancer as a "possible human carcinogen." Concerns about the potential vulnerability of children to radio frequency (RF) fields have been raised because of the potentially greater susceptibility of their developing nervous systems; in addition, their brain tissue is more conductive, RF penetration is greater relative to head size, and they will have a longer lifetime of exposure than adults. To evaluate information relevant to

children's sensitivity to both ELF and RF EMFs and to identify research needs, the World Health Organization held an expert workshop in Istanbul, Turkey, in June 2004. This article is based on discussions from the workshop and provides background information on the development of the embryo, fetus, and child, with particular attention to the developing brain; an outline of childhood susceptibility to environmental toxicants and childhood diseases implicated in EMF studies; and a review of childhood exposure to EMFs. It also includes an assessment of the potential susceptibility of children to EMFs and concludes with a recommendation for additional research and the development of precautionary policies in the face of scientific uncertainty

- (227) Goldsmith JR. Epidemiologic evidence relevant to radar (microwave) effects. *Environ Health Perspect.* 1997;105 Suppl 6:1579-87.:1579-1587.
Abstract: Public and occupational exposures to microwave (RF) are of two main types. The first type of exposures are those connected with military and industrial uses and, to some extent broadcast exposures. It is this type that most of the data cited in this study draw upon. The second type, cellular telephones and their associated broadcast requirements, have raised concerns about current exposures because of their increasingly widespread use. Four types of effects were originally reported in multiple studies: increased spontaneous abortion, shifts in red and white blood cell counts, increased somatic mutation rates in lymphocytes, and increased childhood, testicular, and other cancers. In addition, there is evidence of generalized increased disability rates from a variety of causes in one study and symptoms of sensitivity reactions and lenticular opacity in at least one other. These findings suggest that RF exposures are potentially carcinogenic and have other health effects. Therefore, prudent avoidance of unneeded exposures is recommended as a precautionary measure. Epidemiologic studies of occupational groups such as military users and air traffic controllers should have high priority because their exposures can be reasonably well characterized and the effects reported are suitable for epidemiologic monitoring. Additional community studies are needed
- (228) Hocking B. Microwave sickness: a reappraisal. *Occup Med (Lond).* 2001;51:66-69.
Abstract: Microwave sickness (MWS) has been a disputed condition. The syndrome involves the nervous system and includes fatigue, headaches, dysaesthesia and various autonomic effects in radiofrequency radiation workers. This paper describes the early reports of the syndrome from Eastern Europe and notes the scepticism expressed about them in the West, before considering comprehensive recent reports by Western specialists and a possible neurological basis for the condition. It is concluded that MWS is a medical entity which should be recognized as a possible risk for radiofrequency radiation workers
- (229) Hocking B. Mobile phone use and risk of acoustic neuroma. *Br J Cancer.* 2006;94:1350-1353.
- (230) Hocking B, Westerman R. Neurological effects of radiofrequency radiation. *Occup Med (Lond).* 2003;53:123-127.
Abstract: BACKGROUND: The health effects of radiofrequency radiation (RFR) and the adequacy of the safety standards are a subject of debate. One source of human data is case reports regarding peripheral neurological effects of RFR, mainly noxious sensations or dysaesthesiae. AIM: To investigate health effects, neurophysiological mechanisms and safety levels for RFR. METHODS: We conducted a literature search for case reports and case series associated with mobile phone technology as well as other RFR sources using specific search terms on PubMed. RESULTS: We identified 11 original articles detailing case reports or case series and matching the search criteria. Five of the identified papers were written by at least one

of the authors (B.H. or R.W.). CONCLUSIONS: Cases have arisen after exposure to much of the radiofrequency range. In some cases, symptoms are transitory but lasting in others. After very high exposures, nerves may be grossly injured. After lower exposures, which may result in dysaesthesia, ordinary nerve conduction studies find no abnormality but current perception threshold studies have found abnormalities. Only a small proportion of similarly exposed people develop symptoms. The role of modulations needs clarification. Some of these observations are not consistent with the prevailing hypothesis that all health effects of RFR arise from thermal mechanisms

- (231) Kundi M. Re: "cellular telephone use and risk of acoustic neuroma". *Am J Epidemiol.* 2004;160:923-924.
- (232) Schuz J, Bohler E, Berg G et al. Cellular phones, cordless phones, and the risks of glioma and meningioma (Interphone Study Group, Germany). *Am J Epidemiol.* 2006;163:512-520.
Abstract: The widespread use of cellular telephones has generated concern about possible adverse health effects, particularly brain tumors. In this population-based case-control study carried out in three regions of Germany, all incident cases of glioma and meningioma among patients aged 30-69 years were ascertained during 2000-2003. Controls matched on age, gender, and region were randomly drawn from population registries. In total, 366 glioma cases, 381 meningioma cases, and 1,494 controls were interviewed. Overall use of a cellular phone was not associated with brain tumor risk; the respective odds ratios were 0.98 (95% confidence interval (CI): 0.74, 1.29) for glioma and 0.84 (95% CI: 0.62, 1.13) for meningioma. Among persons who had used cellular phones for 10 or more years, increased risk was found for glioma (odds ratio = 2.20, 95% CI: 0.94, 5.11) but not for meningioma (odds ratio = 1.09, 95% CI: 0.35, 3.37). No excess of temporal glioma ($p = 0.41$) or meningioma ($p = 0.43$) was observed in cellular phone users as compared with nonusers. Cordless phone use was not related to either glioma risk or meningioma risk. In conclusion, no overall increased risk of glioma or meningioma was observed among these cellular phone users; however, for long-term cellular phone users, results need to be confirmed before firm conclusions can be drawn
- (233) Hardell L, Hansson MK. Mobile phone use and risk of acoustic neuroma: results of the interphone case-control study in five North European countries. *Br J Cancer.* 2006;94:1348-1349.
- (234) Hardell L, Hansson MK, Sandstrom M, Carlberg M, Hallquist A, Pahlson A. Vestibular schwannoma, tinnitus and cellular telephones. *Neuroepidemiology.* 2003;22:124-129.
Abstract: Cases with tinnitus after using analogue cellular telephones are presented. An increased odds ratio of 3.45, 95% confidence interval (CI) 1.77-6.76, was found for vestibular schwannoma (VS) associated with the use of analogue cell phones. During the time period 1960-1998, the age-standardized incidence of VS in Sweden significantly increased yearly by +2.53% (CI 1.71-3.35). A significant increase in the incidence of VS was only found for the latter of the two time periods 1960-1979 and 1980-1998. For all other brain tumors taken together, the incidence significantly increased yearly by +0.80% (CI 0.59-1.02) for the time period 1960-1998, although the increase was only significant for benign tumors other than VS during 1960-1979
- (235) Hardell L, Mild KH, Carlberg M. Further aspects on cellular and cordless telephones and brain tumours. *Int J Oncol.* 2003;22:399-407.
Abstract: We included in a case-control study on brain tumours and mobile and cordless

telephones 1,617 patients aged 20-80 years of both sexes diagnosed during January 1, 1997 to June 30, 2000. They were alive at the study time and had histopathology verified brain tumour. One matched control to each case was selected from the Swedish Population Register. The study area was the Uppsala-Orebro, Stockholm, Linkoping and Goteborg medical regions of Sweden. Exposure was assessed by a questionnaire that was answered by 1,429 (88%) cases and 1,470 (91%) controls. In total use of analogue cellular telephones gave an increased risk with odds ratio (OR)=1.3, 95% confidence interval (CI)=1.04-1.6, whereas digital and cordless phones did not overall increase the risk significantly. Ipsilateral use of analogue phones gave OR=1.7, 95% CI=1.2-2.3, digital phones OR=1.3, 95% CI=1.02-1.8 and cordless phones OR=1.2, 95% CI=0.9-1.6. The risk for ipsilateral use was significantly increased for astrocytoma for all studied phone types, analogue phones OR=1.8, 95% CI=1.1-3.2, digital phones OR=1.8, 95% CI=1.1-2.8, cordless phones OR=1.8, 95% CI=1.1-2.9. Use of a telephone on the opposite side of the brain was not associated with a significantly increased risk for brain tumours. Regarding anatomical area of the tumour and exposure to microwaves, the risk was increased for tumours located in the temporal area on the same side of the brain that was used during phone calls, significantly so for analogue cellular telephones OR=2.3, 95% CI=1.2-4.1. For acoustic neurinoma OR=4.4, 95% CI=2.1-9.2 was calculated among analogue cellular telephone users. When duration of use was analysed as a continuous variable in the total material, the risk increased per year for analogue phones with OR=1.04, 95% CI=1.01-1.08. For astrocytoma and ipsilateral use the trend was for analogue phones OR=1.10, 95% CI=1.02-1.19, digital phones OR=1.11, 95% CI=1.01-1.22, and cordless phones OR=1.09, 95% CI=1.01-1.19. There was a tendency of a shorter tumour induction period for ipsilateral exposure to microwaves than for contralateral, which may indicate a tumour promotor effect

- (236) Hardell L, Mild KH, Carlberg M, Hallquist A. Cellular and cordless telephone use and the association with brain tumors in different age groups. *Arch Environ Health*. 2004;59:132-137. Abstract: The authors' case-control study on the possible association between brain tumors and mobile and cordless telephone use included 1,617 patients and 1,617 controls. A questionnaire was answered by 1,429 (88%) cases and 1,470 (91%) controls. Use of analog cellular telephones yielded an odds ratio (OR) for brain tumors of 1.31, 95% confidence interval (CI) = 1.04-1.64, increasing for ipsilateral use to OR = 1.65, 95% CI = 1.19-2.30. The authors found the highest risk for the 20-29-yr age group, with OR = 5.91, 95% CI = 0.63-55 for ipsilateral use of analog phones. The highest risks were associated with >5-year latency period in the 20-29-yr age group for analog phones (OR = 8.17, 95% CI = 0.94-71), and cordless phones (OR = 4.30, 95% CI = 1.22-15)
- (237) Hardell L, Carlberg M, Mild KH. Case-control study of the association between the use of cellular and cordless telephones and malignant brain tumors diagnosed during 2000-2003. *Environ Res*. 2006;100:232-241. Abstract: We performed a case-control study on the use of cellular and cordless telephones and the risk for brain tumors diagnosed during 2000-2003. We report the results for malignant brain tumors with data from 317 cases (88%) and 692 controls (84%). The use of analog cellular phones yielded odds ratio (OR) of 2.6 and a 95% confidence interval (CI) of 1.5-4.3, increasing to OR=3.5 and 95% CI=2.0-6.4 with a >10-year latency period. Regarding digital cellular telephones, the corresponding results were OR=1.9, 95% CI=1.3-2.7 and OR=3.6, 95% CI=1.7-7.5, respectively. Cordless telephones yielded OR=2.1, 95% CI=1.4-3.0, and with a >10-year latency period, OR=2.9, 95% CI=1.6-5.2. The OR increased with the cumulative number of hours of use and was highest for high-grade astrocytoma. A somewhat increased risk was also

found for low-grade astrocytoma and other types of malignant brain tumors, although not significantly so. In multivariate analysis, all three phone types studied showed an increased risk

- (238) Institute of Biomedical Engineering Technology. Electromagnetic Interference: Causes and Concerns in the Health Care Environment. IBET is administered by the Applied Science Technologists and Technicians of British Columbia (ASTTBC) All professional Biomedical Engineering Technologists and Technicians registered with the ASTTBC are members of IBET. 2007. available from <http://ibet.asttbc.org/>
Abstract: In the past 15 years there has been a dramatic increase in the number of radio frequency emission sources that have entered medical treatment areas. Personal computers, digital pagers, hand-held radios, cellular phones, and wireless input devices have all become more prevalent in the contemporary clinical environment. Because of the productivity gains these devices provide, it is unlikely that the use of electronic instrumentation and wireless technologies will diminish-in fact greater uses are projected.
Along with the benefits these devices provide, they also create a greater opportunity for increased electromagnetic interference among devices. It is important that engineering and professional staff are aware of some of the complex interactions these devices can create. Managing this emerging problem should be a concern for the medical community. Engineering staff should be able to communicate effectively with medical staff, patients, and visitors regarding potential interactions and how to recognize them and mitigate their consequences. *This article is part of the Healthcare Facilities Management Series as put out by the American Society of Hospital Engineering of the American Hospital Association*
- (239) World Health Organization. 2006 WHO Research Agenda for Radio Frequency Fields. World Health Organization . 2006. http://www.who.int/peh-emf/research/rf_research_agenda_2006.pdf
- (240) Maisch D, Podd J, and Rapley B. Changes in Health Status in a Group of CFS and CF Patients Following Removal of Excessive 50 Hz Magnetic Field Exposure. Journal of Australian College of Nutritional & Environmental Medicine 21[1], 15-19. 2002. http://www.acnem.org/journal/pdf_files/21-1_april_2002/21-1-health_of_cfs_patients_on_emf_removal.pdf
Abstract: In December 1998 a paper published in the ACNEM *Journal* examined the hypothesis that prolonged exposure to excessive 50 Hz (power line frequency) magnetic fields may act as an immune system stressor giving rise to symptoms similar to those reported in Chronic Fatigue Syndrome (CFS) or Chronic Fatigue (CF).¹ This paper was based on a number of case histories, most notably a well-documented Workcare Compensation case (Melbourne, 1991). Here, a group of female office workers developed CFS-like symptoms when working in a room with strong 50 Hz magnetic fields emitted from an electrical substation immediately below the floor.² The present paper briefly reports the results of a small-scale pilot study utilising 49 subjects suffering from CFS or ongoing CF, who were exposed to varying strength magnetic fields in their home environment. Some subjects were found to have prolonged exposure to magnetic fields >2 mG (milliGauss), which was used as a benchmark level. These subjects (Group A) were provided with advice and assistance regarding reducing their exposure level. The remainder of the subjects (Group B: <2 mG exposure level) were given no such advice or assistance. Changes in health status in both groups were recorded over a 6-month period. Results from the data collected at the start of the study showed no relationship between magnetic field strength and CFS/CF symptom severity. However, the majority of Group A subjects reported an improvement in symptoms and a marked improvement in sleep patterns,

possibly due to the decrease in exposure. These results are discussed in the context of previous research showing disturbed sleep in the presence of magnetic fields. Such disturbances may come about through the effect of magnetic fields on melatonin secretion, a hormone involved in circadian functioning.

- (241) Arendt J. Melatonin and human rhythms. *Chronobiol Int.* 2006;23:21-37.
Abstract: Melatonin signals time of day and time of year in mammals by virtue of its pattern of secretion, which defines 'biological night.' It is supremely important for research on the physiology and pathology of the human biological clock. Light suppresses melatonin secretion at night using pathways involved in circadian photoreception. The melatonin rhythm (as evidenced by its profile in plasma, saliva, or its major metabolite, 6-sulphatoxymelatonin [aMT6s] in urine) is the best peripheral index of the timing of the human circadian pacemaker. Light suppression and phase-shifting of the melatonin 24 h profile enables the characterization of human circadian photoreception, and circulating concentrations of the hormone are used to investigate the general properties of the human circadian system in health and disease. Suppression of melatonin by light at night has been invoked as a possible influence on major disease risk as there is increasing evidence for its oncostatic effects. Exogenous melatonin acts as a 'chronobiotic.' Acutely, it increases sleep propensity during 'biological day.' These properties have led to successful treatments for several circadian rhythm disorders. Endogenous melatonin acts to reinforce the functioning of the human circadian system, probably in many ways. The future holds much promise for melatonin as a research tool and as a therapy for various conditions
- (242) Roberts JE. Update on the positive effects of light in humans. *Photochem Photobiol.* 2005;81:490-492.
Abstract: The adverse effects of sunlight, from melanoma to cataracts, are well known and frequently reported (1). However, because humans evolved under sunlight, it is not surprising that there are many positive effects of light on human health. Light that reaches the human eye has two fundamental biological functions: regulation of the visual cycle and of circadian rhythm. We report here the most recent developments in both of these areas
- (243) Kauppila A, Pakarinen A, Kirkinen P, Makila U. The effect of season on the circulating concentrations of anterior pituitary, ovarian and adrenal cortex hormones and hormone binding proteins in the subarctic area; evidence of increased activity of the pituitary-ovarian axis in spring. *Gynecol Endocrinol.* 1987;1:137-150.
Abstract: To evaluate the effects of season on the function of the pituitary-ovarian axis and the adrenal cortex in a northern area with great seasonal variation in the length of daylight, 10 healthy women were investigated over 1 menstrual cycle in spring (May-June), autumn (August-September), early winter (November-December) and late winter (February-March). Serum concentrations of LH, FSH, prolactin, estradiol, progesterone, total and free testosterone, cortisol, sex hormone binding globulin (SHBG) and cortisol binding globulin (CBG) were measured, and the indices of free estradiol (FEI), free androgen (FAI) and free cortisol (FCI) were calculated on cycle days 3-4, 6-7, 10-11, on the presumed day of ovulation, and 6-7 and 9-10 days after the presumed ovulation. Spring was the season that most significantly differed from the other seasons. It was characterized by a significantly decreased concentration of SHBG and an increased FAI throughout the whole menstrual cycle, an increased FSH concentration during the follicular phase, significantly increased estradiol concentration and an increased FEI, and significantly decreased concentrations of FSH and LH during the luteal phase of the cycle. The concentration of cortisol and the FCI were significantly increased in the

autumn compared with late winter, both seasons having similar day-length. The present data demonstrate that spring, with a long photoperiod, seems to be associated with increased pituitary-ovarian axis activity and androgenic activity, whereas adrenal cortex function did not show any association with day-length

- (244) Rea MS, Figueiro MG, Bullough JD, Bierman A. A model of phototransduction by the human circadian system. *Brain Res Brain Res Rev.* 2005;50:213-228.
Abstract: The absolute and spectral sensitivities to light by the human circadian system, measured through melatonin suppression or phase shifting response, are beginning to emerge after a quarter century of active research. The present paper outlines a hypothesized model of human circadian phototransduction that is consistent with the known neuroanatomy and physiology of the human visual and circadian systems. Spectral opponency is fundamental to the model, providing a parsimonious explanation of some recently published data. The proposed model offers a framework for hypothesis testing and subsequent discussion of the practical aspects of architectural lighting with respect to light and health
- (245) Genuis SJ. Keeping your sunny side up. How sunlight affects health and well-being. *Can Fam Physician.* 2006;52:422-3, 429-31.:422-431.
- (246) Kuller R, Laike T. The impact of flicker from fluorescent lighting on well-being, performance and physiological arousal. *Ergonomics.* 1998;41:433-447.
Abstract: In working environments all over the world, fluorescent tubes are by far the dominating light source. Still, there have been very few studies on the impact of the non-visible flicker from fluorescent tubes. The purpose of the study was to compare the impact on subjective well-being, performance and physiological arousal of fluorescent light powered by conventional and high-frequency ballasts. Thirty-seven healthy males and females were subjected to either condition in a laboratory office on two separate occasions with 1 week in between. Although the methodology was quite extensive, only a few general effects were observed. However, when the light was powered by the conventional ballasts, individuals with high critical flicker fusion frequency (CFF) responded with a pronounced attenuation of EEG alpha waves, and an increase in speed and decrease in accuracy of performance. These results may be understood in terms of heightened arousal in the central nervous system in response to the pronounced light modulation caused by the conventional ballasts. In order to alleviate this potential stress source, it is recommended that fluorescent lighting be powered by electronic high-frequency ballasts of good quality
- (247) Marks TA, Ratke CC, English WO. Stray voltage and developmental, reproductive and other toxicology problems in dogs, cats and cows: a discussion. *Vet Hum Toxicol.* 1995;37:163-172.
Abstract: Ten years ago, after 3 y of investigations, attempts to determine the cause(s) of reproductive and developmental problems at a dog kennel in Allegan County, MI were suspended. This kennel had lost more than 120 litters of Shetland Sheepdogs (Shelties) over the preceding 12 y; many of the puppies that died were deformed as were several that survived. Similar effects occurred in Persian cats, although on a smaller scale, and later in German Shepherds and Golden Retrievers. Such problems began after drilling a deeper water well and the building of a new kennel of concrete and metal fencing in 1969. Prior to that time the kennel owner had successfully bred and raised at least 15 litters/y of mostly Shelties in an old wooden chicken coop. Health problems in the kennel owner prevented her from breeding dogs in the late 1980's. She gradually resumed a more regular breeding schedule in 1989, initially with some success. However, in 1992 reproductive problems returned. Female dogs ceased cycling

or had abnormal "unbreedable" seasons. Sperm checks revealed a lack of sperm in four males. Concurrently, neither the Persian nor mongrel female cats in the kennel showed signs of cycling. Two dairy farmers in Allegan County, who reportedly had similar health, reproductive and management concerns in cows, were contacted. Tests performed at these dairy farms had revealed the presence of what has commonly been called stray voltage. Equipment brought by the farmers to the kennel revealed the presence of AC and DC currents on the premises, which was later confirmed by a Staff Engineer of the Michigan Public Service Commission (PSC). Such current was detected even when the electrical power to the premises was shut off. For example, 2.45 volts AC and -0.150 volts DC were detected at the well head, with variable amounts detected at various locations in the kennel. The current was not constant, with transients (spikes) frequently detected. Similar problems were evident in Van Buren County at a recently constructed kennel about 15 miles south of the kennel in Allegan County. Shortly after moving to the property, health problems not previously experienced by the breeder began cropping up in the dogs. Experts from the power company, the PSC, and 2 independent consultants have taken a variety of measurements on the property. The tests confirmed the presence of stray voltage (AC and DC) with periodic voltage spikes, as well as electromagnetic fields and electric fields. None of the extensive tests have proven the property owner to be at fault.(ABSTRACT TRUNCATED AT 400 WORDS)

- (248) Hultgren J. Small electric currents affecting farm animals and man: a review with special reference to stray voltage. I. Electric properties of the body and the problem of stray voltage. *Vet Res Commun.* 1990;14:287-298.
Abstract: The literature on the electrical properties of the body and sensitivity to steady electric current in humans and farm animals is reviewed and the problem of stray voltage is examined. Stray voltage poses a problem to animal health and protection in cattle and pigs and possibly also in other animals. Dairy cattle can perceive alternating currents exceeding 1 mA between the mouth and all four hooves. Behavioural effects in cows usually occur above 3 mA. In practice, the major influence on dairy cows appears to be behavioural. In experimental research on sensitivity to electric current, the effects studied should be related primarily to the actual current densities or electric fields in the affected tissues rather than to the total voltages applied. Under normal conditions, herdsman are less likely to be affected by stray voltage than their animals
- (249) Hultgren J. Small electric currents affecting farm animals and man: a review with special reference to stray voltage. II. Physiological effects and the concept of stress. *Vet Res Commun.* 1990;14:299-308.
Abstract: The literature on the influence of small, steady electric currents on animal health, especially cardiovascular and endocrinological functions and milk let-down, and the effects on milk production is reviewed, with special reference to the problem of stray voltage. Direct physiological effects in cows may occur above 4 mA. How the long-term effects may contrast with the acute effects is not known. Habituation may occur. The altered behaviour and physiological changes due to exposure to stray voltage may be termed a stress response. The type of stress most likely to be encountered is chronic. Whether or not stress occurs depends on the timing and context of exposure and on individual cognition. Hence stray voltage may threaten farm animal health and production wherever modern animal housing is applied
- (250) Mairs RJ, Hughes K, Fitzsimmons S et al. Microsatellite analysis for determination of the mutagenicity of extremely low-frequency electromagnetic fields and ionising radiation in vitro. *Mutat Res.* 2007;626:34-41.

Abstract: Extremely low-frequency electromagnetic fields (ELF-EMF) have been reported to induce lesions in DNA and to enhance the mutagenicity of ionising radiation. However, the significance of these findings is uncertain because the determination of the carcinogenic potential of EMFs has largely been based on investigations of large chromosomal aberrations. Using a more sensitive method of detecting DNA damage involving microsatellite sequences, we observed that exposure of UVW human glioma cells to ELF-EMF alone at a field strength of 1 mT (50 Hz) for 12 h gave rise to 0.011 mutations/locus/cell. This was equivalent to a 3.75-fold increase in mutation induction compared with unexposed controls. Furthermore, ELF-EMF increased the mutagenic capacity of 0.3 and 3 Gy gamma-irradiation by factors of 2.6 and 2.75, respectively. These results suggest not only that ELF-EMF is mutagenic as a single agent but also that it can potentiate the mutagenicity of ionising radiation. Treatment with 0.3 Gy induced more than 10 times more mutations per unit dose than irradiation with 3 Gy, indicating hypermutability at low dose

(251) Mild KH, Mattsso MO, Hardell L, Bowman JD, Kundi M. Occupational carcinogens: ELF MFs. *Environ Health Perspect.* 2005;113:A726-A727.

(252) de VF, van DH, Engels H, Kromhout H. Exposure, health complaints and cognitive performance among employees of an MRI scanners manufacturing department. *J Magn Reson Imaging.* 2006;23:197-204.

Abstract: PURPOSE: To assess sensory effects and other health complaints that are reported by system testers working near magnetic resonance imaging (MRI) magnets, realizing that it is believed that exposure up to 8 T is safe for humans. MATERIALS AND METHODS: Levels of exposure to static magnetic fields (SMFs), movement speed during exposure, health complaints, and cognitive performance among employees in an MRI-manufacturing department and at a reference department have been analyzed. Mercury concentrations in urine samples were determined to analyze whether they depend on exposure to SMFs. RESULTS: Average exposure of system testers was 25.9 mT/8 hours at a 1.0-T system and 40.4 mT/8 hours at a 1.5-T system. Vertigo, metallic taste, and concentration problems were more reported among workers of MRI-fabrication than in the reference department. Cognitive performance was tested outside the SMF, and no significant changes were detected. CONCLUSION: This study suggests that any effects on cognitive functions are acute and transient and disappear rapidly after exposure has ended. All complaints, except for headaches, were more frequently reported by "fast movers" than by "slow movers," and depended on field strength and duration of exposure. Mercury-levels in urine were not affected

(253) Hardell L, Mild KH, Carlberg M, Soderqvist F. Tumour risk associated with use of cellular telephones or cordless desktop telephones. *World J Surg Oncol.* 2006;4:74.:74.

Abstract: ABSTRACT: BACKGROUND: The use of cellular and cordless telephones has increased dramatically during the last decade. There is concern of health problems such as malignant diseases due to microwave exposure during the use of these devices. The brain is the main target organ. METHODS: Since the second part of the 1990's we have performed six case-control studies on this topic encompassing use of both cellular and cordless phones as well as other exposures. Three of the studies concerned brain tumours, one salivary gland tumours, one non-Hodgkin lymphoma (NHL) and one testicular cancer. Exposure was assessed by self-administered questionnaires. RESULTS: Regarding acoustic neuroma analogue cellular phones yielded odds ratio (OR) = 2.9, 95 % confidence interval (CI) = 2.0-4.3, digital cellular phones OR = 1.5, 95 % CI = 1.1-2.1 and cordless phones OR = 1.5, 95 % CI = 1.04-2.0. The corresponding results were for astrocytoma grade III-IV OR = 1.7, 95 % CI = 1.3-2.3; OR =

1.5, 95 % CI = 1.2-1.9 and OR = 1.5, 95 % CI = 1.1-1.9, respectively. The ORs increased with latency period with highest estimates using > 10 years time period from first use of these phone types. Lower ORs were calculated for astrocytoma grade I-II. No association was found with salivary gland tumours, NHL or testicular cancer although an association with NHL of T-cell type could not be ruled out. CONCLUSION: We found for all studied phone types an increased risk for brain tumours, mainly acoustic neuroma and malignant brain tumours. OR increased with latency period, especially for astrocytoma grade III-IV. No consistent pattern of an increased risk was found for salivary gland tumours, NHL, or testicular cancer

- (254) Schoemaker MJ, Swerdlow AJ, Ahlbom A et al. Mobile phone use and risk of acoustic neuroma: results of the Interphone case-control study in five North European countries. *Br J Cancer*. 2005;93:842-848.
Abstract: There is public concern that use of mobile phones could increase the risk of brain tumours. If such an effect exists, acoustic neuroma would be of particular concern because of the proximity of the acoustic nerve to the handset. We conducted, to a shared protocol, six population-based case-control studies in four Nordic countries and the UK to assess the risk of acoustic neuroma in relation to mobile phone use. Data were collected by personal interview from 678 cases of acoustic neuroma and 3553 controls. The risk of acoustic neuroma in relation to regular mobile phone use in the pooled data set was not raised (odds ratio (OR) = 0.9, 95% confidence interval (CI): 0.7-1.1). There was no association of risk with duration of use, lifetime cumulative hours of use or number of calls, for phone use overall or for analogue or digital phones separately. Risk of a tumour on the same side of the head as reported phone use was raised for use for 10 years or longer (OR = 1.8, 95% CI: 1.1-3.1). The study suggests that there is no substantial risk of acoustic neuroma in the first decade after starting mobile phone use. However, an increase in risk after longer term use or after a longer lag period could not be ruled out
- (255) Maisch D. Mobile Phone Use: it's time to take precautions. *Journal of Australasian College of Nutritional & Environmental Medicine*. 2002;21:3-10.
Abstract: **Recommendations**
A. For the reasons mentioned above, children should be discouraged from using mobile (and cordless) phones as their developing bodies can be more prone to radiation damage;
B. Incoming mobile phone calls should be kept as brief as possible and returned on a conventional wired phone;
C. When a mobile phone is being used it should be held away from the body as much as practical, not pressed against the head or clipped to a belt. Some phones have an in-built loudspeaker/microphone that allows conversations with the antenna held away from the head;
D. As much as possible, use pagers or the mobile phone's message bank service and return calls on a conventional phone;
E. There have been conflicting reports that use of hands-free kits with mobile phones may still expose the user to microwave emissions due to a "coupling effect" with the earpiece lead. The extent of this problem very much depends upon the type of cellular phone used but generally hand free kits do greatly reduce exposure. Hands free kits are now available for most cell phones, incorporating ferrite filters in the wire to eliminate any microwave emissions going into the ear piece. They should be used in preference to the "non-filtered" ones.
- (256) International Association of Fire Fighters and Division of Occupational Health, Safety and Medicine. Position on the Health Effects from Radio Frequency/Microwave (RF/MW) Radiation in Fire Department Facilities from Base Stations for Antennas and Towers for the

Conduction of Cell Phone Transmissions. 2006. available from <http://www.iaff.org/safe/content/celltower/celltowerfinal.htm>

Abstract: The International Association of Fire Fighters' position on locating cell towers commercial wireless infrastructure on fire department facilities, as adopted by its membership in August 2004 (1), is that the IAFF oppose the use of fire stations as base stations for towers and/or antennas for the conduction of cell phone transmissions until a study with the highest scientific merit and integrity on health effects of exposure to low-intensity RF/MW radiation is conducted and it is proven that such sitings are not hazardous to the health of our members. Further, the IAFF is investigating funding for a U.S. and Canadian study that would characterize exposures from RF/MW radiation in fire houses with and without cellular antennae, and examine the health status of the fire fighters as a function of their assignment in exposed or unexposed fire houses. Specifically, there is concern for the effects of radio frequency radiation on the central nervous system (CNS) and the immune system, as well as other metabolic effects observed in preliminary studies.

It is the belief of some international governments and regulatory bodies and of the wireless telecommunications industry that no consistent increases in health risk exist from exposure to RF/MW radiation unless the intensity of the radiation is sufficient to heat body tissue.

However, it is important to note that these positions are based on non-continuous exposures to the general public to low intensity RF/MW radiation emitted from wireless telecommunications base stations. Furthermore, most studies that are the basis of this position are at least five years old and generally look at the safety of the phone itself. IAFF members are concerned about the effects of living directly under these antenna base stations for a considerable stationary period of time and on a daily basis. There are established biological effects from exposure to low-level RF/MW radiation. Such biological effects are recognized as markers of adverse health effects when they arise from exposure to toxic chemicals for example. The IAFF's efforts will attempt to establish whether there is a correlation between such biological effects and a health risk to fire fighters and emergency medical personnel due to the siting of cell phone antennas and base stations at fire stations and facilities where they work.

(257) Boyd DR. The Food We Eat. David Suzuki Foundation . 2006.

<http://www.davidsuzuki.org/files/SWAG/DSF-HEHC-Food1.pdf> available from <http://www.davidsuzuki.org/WOL/Publications.asp>

Abstract: The comparative analysis reveals that as of July 2006, there are 60 active ingredients, used in 1,130 pesticide products, which continue to be registered for use in Canada despite having been banned in other western industrialized nations because of health and environmental concerns. The majority of these pesticides have been prohibited in one or more European nations.

Canadian MRLs [maximum residue levels] appear to be among the weakest in the industrialized world in protecting the health of citizens from the negative effects of pesticides in food products. In theory, both Canada and the European Union endorse the precautionary principle, which means "where there are threats of serious or irreversible damage, lack of full scientific certainty should not be used as a reason for postponing measures to prevent environmental degradation." 61 Most current Canadian environmental legislation incorporates the precautionary principle, and the Supreme Court of Canada has endorsed it.62 In practice however, when it comes to protecting human health from the adverse effects of pesticides, the EU is applying the precautionary principle while Canada is not.

(258) Indoor Environments Division Office of Radiation and Indoor Air Office of Air and Radiation United States Environmental Protection Agency. Energy Cost and IAQ Performance of

Ventilation Systems and Controls - Project Report # 7 The Cost of Protecting Indoor Environmental Quality During Energy Efficiency Projects for Office and Education Buildings - Integrating Indoor Environmental Quality with Energy Efficiency. USA Environmental Protection Agency . 2000.

[http://www.epa.gov/iaq/largeblids/resources/\(2\)%20Energy%20Cost%20and%20IAQ/Project%20Report%207.PDF](http://www.epa.gov/iaq/largeblids/resources/(2)%20Energy%20Cost%20and%20IAQ/Project%20Report%207.PDF) available from <http://www.epa.gov>

Abstract: This report suggests that indoor environmental quality need not be detractor to achieving substantial energy savings in buildings. Energy savings of 31% - 45% were achieved in a staged energy retrofit program which was designed to prevent degradation of IEQ. Further savings in the range of 5% - 15% are possible through commissioning (not modeled) plus 12% or more from reduced lighting and office equipment use during unoccupied hours. Instituting all the controls needed to meet the outdoor air and humidity requirements of ASHRAE Standard 62-1999 increased the energy cost of the Stage 4 retrofitted building by only 3% - 4% in the office building, but by 5% - 14% in the education building. However, when measured against the base (pre-retrofitted) building, these increases mean that the energy savings foregone because of ASHRAE Standard 62-1999 requirements were only 2% -3% for the office, and 3% - 9% for the education building. Similarly, the outdoor air and humidity requirements limited the degree to which chillers and boilers could be downsized. However, the use of energy recovery technology is likely to either eliminate or substantially reduce that penalty, and allow for greater downsizing of chillers and boilers.

- (259) New Zealand Association of Hairdressers Inc. Guide to occupational safety and health for the hairdressing industry. 1997. <http://www.osh.govt.nz/order/catalogue/ipp/hairdressers.pdf>
Abstract: The New Zealand Association of Hairdressers has been concerned at the injuries and health problems among hairdressers which are directly attributable to work practices in the industry. This guide has been written in consultation with the hairdressing industry, and offers practical information and advice on managing health and safety in the salon.
- (260) Connecticut Department of Public Health - Division of Environmental Epidemiology & Occupational Health. Hairdressers and Work-related Respiratory Disease. 1998. <http://www.dph.state.ct.us/Publications/BRS/EOHA/news898.pdf>
Abstract: There are over one half-million hairdressers working in the United States and 23,000 licensed hairdressers in CT. Hairdressers are exposed to many different chemicals in the workplace which can result in health problems, such as respiratory and skin disorders. Approximately 20% of hairdressers leave the profession for health reasons. This article will focus on respiratory diseases that affect the hairdressing profession, particularly occupational asthma and lung disease possibly associated with hair spray.
- (261) Bowman JK, Kelsh MA, and Kaune WT. Manual for Measuring Occupational Electric and Magnetic Field Exposures. NIOSH . 1998. available from <http://www.cdc.gov/niosh/98-154pd.html>
Abstract: This NIOSH technical document is a reference work for industrial hygienists and researchers who measure occupational exposures to electric and magnetic fields (EMF). The Manual contains 16 exposure measurement protocols which have been used successfully in EMF epidemiologic studies and NIOSH's health hazard evaluations. The protocols are summarized and critiqued in a standard format, and are published with suggestions for developing measurement methods for new applications. The Manual includes an extensive index and glossary.

- (262) Kats G. Greening America's Schools Costs and Benefits. www.cap-e.com . 2006. <http://www.cap-e.com/ewebeditpro/items/O59F9819.pdf>
Abstract: This carefully documented study conclusively demonstrates the financial, environmental, and other benefits of using green technologies in schools. In fact, failure to invest in green technologies is not financially responsible for school systems; the study uses conservative accounting practices to show that investments in green technologies significantly reduce the life-cycle cost of operating school buildings. And the public benefits of green schools are even larger than those that work directly to the financial advantage of schools. These include reductions in water pollution, improved environmental quality, and increased productivity of learning in an improved school environment.
Greening school design is extremely cost-effective. Green schools cost on average almost 2% more, or \$3 more per ft², than conventional schools. The financial benefits of greening schools are about \$70 per ft², more than 20 times as high as the cost of going green. Only a portion of these savings accrue directly to an individual school. Lower energy and water costs, improved teacher retention, and lowered health costs save green schools directly about \$12/ft², about four times the additional cost of going green, and enough to hire an additional full-time teacher. Analysis of the costs and benefits of 30 green schools and use of conservative and prudent financial assumptions provides a clear and compelling case that greening schools today is extremely cost-effective, and represents a fiscally far better design choice. Building green schools is more fiscally prudent and lower risk than continuing to build unhealthy, inefficient schools.
- (263) Environmental Law Institute. Building Healthy, High Performance Schools: A Review of Selected State and Local Initiatives. Washington D.C.All rights reserved.ISBN# 1-58576-069-2, ELI project code 011404 . 2003. http://www.elistore.org/reports_detail.asp?ID=10925
Abstract: Over the past several years, an impressive array of technologies, information, and other resources have been developed to improve the way school buildings are designed and constructed. These tools can be used to change the traditional approach to school building in the United States-an approach that has a considerable negative impact on the natural environment and has produced many facilities that are costly to operate, difficult to maintain, and in some cases, unhealthy for children and staff. With tens of billions of dollars to be invested in school building programs in the coming years, states and school districts have a unique opportunity to use the wealth of information and other resources now available to maximize their investment in school facilities.A new approach to school planning, design, and construction aims to create "high performance" schools- buildings that support the learning process and are healthier, more environmentally responsible, and less expensive to operate. In the best cases, the buildings themselves are interactive tools for learning. Across the country, there are currently many examples of high performance school facilities. This report focuses on state-wide and school-district- wide initiatives that establish a framework for the early, integrated consideration of a wide range of health and environmental goals in new school building projects. These initiatives do not require a specific set of building features, but rather they create a decision-making process to identify design strategies in areas ranging from site planning and resource efficiency to ventilation, daylighting, and material selection.
- (264) Pejtersen J, Brohus H, Hyldgaard CE et al. Effect of renovating an office building on occupants' comfort and health. *Indoor Air*. 2001;11:10-25.
Abstract: An intervention study was performed in a mechanically ventilated office building in which there were severe indoor climate complaints among the occupants. In one part of the building a new heating and ventilation strategy was implemented by renovating the HVAC

system, and a carpet was replaced with a low-emitting vinyl floor material; the other part of the building was kept unchanged, serving as a control. A comprehensive indoor climate investigation was performed before and after the intervention. Over a 2-week period, the occupants completed a daily questionnaire regarding their comfort and health. Physiological examinations of eyes, nose and lungs were performed on each occupant. Physical, chemical and sensory measurements were performed before and after the intervention. The renewal of the flooring material was performed after a sensory test of alternative solutions in the laboratory. Before the floor material was installed in the office building, a full-scale exposure experiment was performed in the laboratory. The new ventilation strategy and renovation of the HVAC system were selected on the basis of laboratory experiments on a full-scale mock-up of a cellular office. The severity of occupants' environmental perceptions and symptoms was significantly reduced by the intervention

- (265) Chao HJ, Schwartz J, Milton DK, Burge HA. The work environment and workers' health in four large office buildings. *Environ Health Perspect.* 2003;111:1242-1248.
Abstract: We conducted a 1-year epidemiologic study in Boston, Massachusetts, beginning May 1997, to examine the associations between environmental factors and office workers' health. We recruited 98 subjects (81 females and 17 males) in 21 offices in four office buildings. We conducted environmental sampling every 6 weeks and concurrently administered detailed questionnaires to collect information on work-related symptoms, psychosocial factors, and perceptions of the office environments. In multivariate analyses, eye irritation was positively correlated with floor dust [odds ratio (OR) = 1.46; 95% confidence intervals (CI), 1.14-1.86] and reported lack of office cleanliness (OR = 1.52; 95% CI, 1.11-2.08). Nonspecific symptoms were positively associated with unidentified chair fungi (OR = 1.87; 95% CI, 1.11-3.15) and several self-reported conditions, including a history of asthma (OR = 3.15; 95% CI, 1.26-7.87), more people in offices (OR = 1.71; 95% CI, 1.16-2.51), lack of office cleanliness (OR = 2.85; 95% CI, 1.72-4.73), and low job satisfaction (OR = 1.72; 95% CI, 1.06-2.81). Upper respiratory symptoms were positively associated with total fungal concentrations recovered from chair dust (OR = 1.35; 95% CI, 1.07-1.70) and the following self-reported conditions: more people in offices (OR = 1.45; 95% CI, 1.01-2.08), lack of office cleanliness (OR = 1.62; 95% CI, 1.15-2.30), and jobs frequently requiring hard work (OR = 1.43; 95% CI, 1.05-1.95). This study emphasizes the importance of maintaining a clean, uncrowded workspace and the importance of chair fungi as a correlate for health effects
- (266) WHO European Centre for Environment and Health. Strategic approaches to indoor air policy-making. World Health Organization . 1999. <http://www.euro.who.int/document/e65523.pdf>
Abstract: Indoor air quality is an important determinant of public health and comfort. This document informs and advises governments, public health authorities and other policy-makers, and representatives of sectors relevant to indoor air quality (IAQ) management, on how to develop and strengthen IAQ policy in order to protect and promote health in the indoor environment. It specifically addresses strategies for the development of IAQ policies for non-industrial buildings such as homes, schools, offices, health care facilities and other public and commercial buildings. Development and implementation of a comprehensive, scientifically sound "action plan" is proposed as a key strategy tool. The document outlines the contents of such an action plan, addresses the roles of public and private sectors in policy implementation, and the roles of various levels of government, industry and research. Summaries of experience in various countries of Europe and in the USA illustrate the current situation and diversity of possible approaches to the improvement of IAQ.